Translation from Bulgarian

REGULATION No. 9 OF 25 APRIL 2006 ON THE ESTABLISHMENT OF A TRANSFUSION HAEMATOLOGY MEDICAL STANDARD

Issued by the Ministry of Health

Promulgated in State Gazette (SG) Issue 42 of 23 May 2006, amended in SG Issue 37 of 8 May 2007, ***amended in SG Issue 92 of 23 November 2010***

Article One. (1) This Regulation establishes a Transfusion Haematology Medical Standard, as presented in the attached annex.

(2) Transfusion haematology is carried out in compliance with the standard referred to in paragraph 1 in all healthcare facilities where transfusion haematology is conducted as a regular procedure.

Additional Provisions

§ 1. For the purposes of this Regulation, the following definitions shall apply:

1. 'Validation' means the establishment of documented evidence providing a high level of security that a particular process will ensure consistent results such as products and activities that meet the predefined requirements and quality parameters;
2. 'Good manufacturing practice' means all elements of an activity that collectively will lead to final products or activities that consistently meet predefined specifications;
3. 'Quarantine' means the physical isolation of blood components or incoming materials (reagents) over a variable period of time while awaiting acceptance, issuance or rejection of the blood components or incoming materials (reagents).
4. "Quality control' means part of a quality assurance programme which consists of retrospective tests or measures that have to produce satisfactory results, before moving on to the next stage of a given process, and which fulfils certain criteria and specifications.

5. ‘Computerised information system’ means a system including the input of data, electronic processing and the output of information to be used either for reporting, automatic control or documentation.
6. ‘Mobile site’ means a temporary or movable place used for the collection of blood and blood components which is in a location outside of the Blood Transfusion Establishments (BTE) or the Blood Transfusion Wards (BTW) at the regional hospitals for active treatment.
7. ‘Quality assurance’ means all the activities from blood collection to distribution made with the object of ensuring that blood and blood components are of the quality required for their intended use.
8. ‘Quality monitoring’ means part of the quality assurance focused on maintaining and improving quality and includes identification and use of indicators for detection of deviations from standards and specifications.
9. ‘Processing’ means any step in the preparation of a blood component that is carried out between the collection of blood and the issuing of a blood component.
10. ‘Issuing’ is provision from a blood transfusion establishment or a blood transfusion ward in a hospital, of blood or blood components for transfusion to a recipient.
11. ‘Quality system’ means the organisational structure, responsibilities, procedures, processes, and resources for implementing quality management.
12. ‘Quality control’ means part of a quality system focused on fulfilling quality requirements.
13. ‘Specification’ means description of the requirements which have to be fulfilled to achieve the required quality standard.
14. ‘Standards’ means the requirements that serve as the basis for comparison against which products and processes are measured in terms of quality and/or quantity.
15. ‘Written procedures (standard operating protocols)’ means controlled documents that describe how specified operations are to be carried out.
16. ‘Quality management’ means the coordinated activities to direct and control an organisation with regard to quality at all levels within the healthcare facility carrying out activities under the Blood, Blood Donation and Blood Transfusion Act (BBDBTA).

Transitional and Final Provisions

§ 2. Healthcare facilities should align their activities with the requirements under Section II, point 4 and Section III, points 3 and 4 of the attached annex within one year from the effective date of this Regulation.

§ 3. This Regulation is issued pursuant to Article 6, paragraph 1 of the Healthcare Facilities Act and pursuant to Article 1, paragraph 4 of the Blood, Blood Donation and Blood Transfusion Act.

§ 4. (New – SG Issue 92 of 2010) The standard and specific equipment and apparatus referred to in the Annex to Article 1, paragraph 1, if impossible to be provided for each clinical structure, should be provided to the healthcare facility in sufficient numbers and types so as to assure the fulfilment of the requirements for competence and volume of work for each structure at the different levels.

Annex to Article 1, paragraph 1

(Amended in State Gazette, Issue 37 of 2007, Amended in SG Issue 92 of 2010)

TRANSFUSION HAEMATOLOGY MEDICAL STANDARD

Section I

Basic characteristics of Transfusion Haematology

1. Definition, main objectives and tasks

1.1 Definition

Transfusion haematology is a major medical field and scientific discipline which includes a set of organised activities for promotion and organisation of voluntary non-remunerated blood donation, and collection, testing, processing, control, storage, distribution and clinical use of blood, blood components and plasma products, planning of and provision for the medical needs of inpatient healthcare facilities and dispensaries where blood and blood

components are supplied under ordinary or emergency conditions, immuno-haematologic testing of patients, haemovigilance.

Transfusion haematology is a scientific field of an interdisciplinary nature, interacting with all other medical fields. At the same time, the activities related to transfusion haematology are so specific that they create a general regulatory framework which is characteristic only of it.

1.2 Main objectives

The main objectives of this scientific field is provision of safe and effective blood components to satisfy medical needs across the country and for production of medicines, provision of immuno-haematologic testing of patients and appropriate clinical use of the blood components.

1.3 Main tasks

The main tasks of transfusion haematology are related to the achievement of some predefined objectives, and more specifically:

1.3.1. Promotion, organisation, recruitment and retention of blood donors;

1.3.2. Selection of donors and collection of blood and blood components;

1.3.3. Processing and testing of blood and blood components;

1.3.4. Process validation;

1.3.5. Storage, issuance and distribution of blood and blood components;

1.3.6. Maintaining a blood component pool;

1.3.7. Immuno-haematologic testing of patients and selection of blood components for each individual patient;

1.3.8. Quality control of activities at BTEs;

1.3.9. Achievement of optimal clinical use of blood and blood components;

1.3.10. Provision of expert systematic counselling and aid as regards the transfusion haematology activities regulated by the Blood, Blood Donation and Blood Transfusion Act;

1.3.11. Organisation of external control of the qualification of the personnel employed at the immuno-haematologic laboratories in the country and the laboratories providing immuno-haematologic services to patients;

1.3.12. Personnel training;

1.3.13. Haemovigilance;

1.4. The National Transfusion Haematology Standard regulates the following:

1.4.1. The main requirements which blood establishments where transfusion haematology activities are performed should meet;

1.4.2. The mandatory (minimum) activities which should be carried out at blood establishments;

1.4.3. The mandatory requirements for available equipment including apparatus, medical devices and consumables for transfusion haematology at the different levels;

1.4.4. The recommended methods and techniques for blood testing and immuno-haematologic testing of patients;

1.4.5. The mandatory requirements for a quality system covering the regulated activities;

1.4.6. The main requirements for the qualifications required for work in this field.

2. Key aspects of Transfusion Haematology

Transfusion Haematology includes the following key aspects:

2.1. Organisation of blood donation and blood transfusion with the following subfields:

2.1.1. promotion of voluntary non-remunerated blood donation;

2.1.2. organisation, planning and information support in the blood transfusion practice;

2.1.3. organisation of blood transfusion;

2.1.4. quality system in the blood transfusion practice.

2.2. Collection, processing, storage and issuing of blood and blood components with the following subfields:

2.2.1. collection of blood and blood components;

2.2.2. blood processing;

2.2.3. storage, issuing and distribution of blood and blood components;

2.3. Laboratory haematology and transfusiology in the following subfields:

2.3.1. haematopoiesis;

2.3.2. immuno-haematology;

2.3.3. special testing of collected blood;

2.3.4. haemostasis.

2.4. Clinical transfusiology with the following subfields:

2.4.1. treatment with blood products;

2.4.2. reactions and complications after administration of blood products;

2.4.3. alternatives to blood transfusion therapy.

3. Qualification requirements for work in this field

A degree in Transfusion Haematology is acquired as specified in Regulation No. 31 of 2001 on postgraduate studies in the healthcare system (SG Issue 64 of 2001).

3.1. Medical expertise:

3.1.1. In transfusion haematology, medical expertise is graded into three levels of complexity:

3.1.1.1. Level 1: carried out by a healthcare professional without a degree and/or by a healthcare professional specialising in transfusion haematology;

3.1.1.2. Level 2: carried out by a healthcare professional in transfusion haematology; involves independent operations in all key aspects of the medical field;

3.1.1.3. Level 3: carried out by healthcare professionals with habilitation qualification to carry out teaching, scientific and advisory activities in the respective key fields and subfields of transfusion haematology.

3.1.2. Heads of wards and laboratories at the Blood Transfusion Establishments (BTE) and heads of wards at the regional hospitals for active treatment with blood transfusion wards (HAT with BTW) may be healthcare professionals with a recognised degree in transfusion haematology. Exceptions are made for healthcare professionals specialising in transfusion haematology, and healthcare professionals with a degree in internal diseases, anaesthesiology, reanimation or immunology, holding a certificate of further qualification in transfusion haematology.

3.1.3. Heads of wards or laboratories at BTAs and heads of BTWs at regional hospitals for active treatment have the following responsibilities:

3.1.3.1. To plan, organise, control and have responsibility for all the operations carried out in the ward / laboratory;

3.1.3.2. To control the quality and timeliness of the operations in compliance with the requirements of the good laboratory and manufacturing practice;

3.1.3.3. To participate in the primary operations of the ward / laboratory;

3.1.3.4. To establish the required organisational ties between the ward / laboratory and other structural units of the healthcare facility;

3.1.3.5. To monitor the technical condition of the laboratory equipment, technical facilities and reagents used;

3.1.3.6. To develop a programme for control of the quality and effectiveness of all operations;

3.1.3.7. To manage the resources at the ward by creating conditions for assigning uniform parts of the workload on the personnel at the ward / laboratory;

3.1.3.8. To give an expert opinion on the supplies of reagents, consumables and equipment, and to control all orders;

3.1.3.9. To manage the postgraduate training and continuous qualification of the healthcare specialists at the ward / laboratory; to develop a programme for qualification of healthcare professionals and laboratory technicians;

3.1.3.10. To organise the participation of healthcare professionals in various associations, by managing the information, innovation and scientific activities at the ward, if the healthcare facility engages in research activity.

3.1.4. The healthcare professional:

3.1.4.1. Carries out independent operations regulated in the standard;

3.1.4.2. Controls manufacturing processes;

3.1.4.3. Controls the activities carried out by biologists, nurses and laboratory technicians;

3.1.4.4. Assures the effectiveness and safety of the operations and processes;

3.1.4.5. Participates in the development and implementation of new methods and technologies;

3.1.4.6. Plans, controls and submits reports on the required medical devices and in vitro medical devices;

3.1.4.7. Assists the head of the structural unit in the preparation of the analyses and reports on the operations, and takes over his/her functions in his/her absence;

3.1.4.8. Provides counselling on each diagnostic and treatment procedure for patients requiring blood transfusion therapy;

3.1.4.9. Participates in healthcare professional and scientific associations.

3.1.5. Healthcare professionals without specialisation and/or healthcare professionals specialising in transfusion haematology:

3.1.5.1. Carry out operations regulated in the standard;

3.1.5.2. Control manufacturing processes;

3.1.5.3. Control the activities carried out by biologists, nurses and laboratory technicians;

3.1.5.4. Assure the effectiveness and safety of the operations and processes;

3.1.5.5. Participate in the development and implementation of new methods and technologies;

3.1.5.6. Plan, control and submit reports on the required medical devices and in vitro medical devices;

3.1.5.7. Assist the head of the structural unit in the preparation of the analyses and reports on the operations, and take over his/her functions in his/her absence;

3.1.5.8. Participate in healthcare professional and scientific associations.

3.2. Pharmacists:

Pharmacists with a Master's Degree may carry out activities related to processing, storage and issuing of blood components, and preparation and storage of in vitro diagnostic devices.

3.3. Biologists with a Master's Degree

Biologists with a Master's Degree may carry out operations related to the promotion and organization of blood donation, testing, control, processing, storage and issuing of blood components. The performance of responsible tasks assigned by the head of a structural unit requires a certificate of further qualification in the respective key area.

3.4. Laboratory technicians:

3.4.1. Have knowledge of all diagnostic methods and equipment included in the list of medical procedures of the unit at which they work;

3.4.2. Observe strictly the standard operating protocols for each diagnostic procedure;

3.4.3. Keep systematic records of all necessary documentation;

3.4.4. Identify the needs of supply of in vitro diagnostic devices and consumables;

3.5. Nurses:

3.5.1. Have knowledge of all procedures included in the list of medical procedures of the unit at which they work;

3.5.2. Observe strictly the standard operating protocols for each procedure; keep systematic records of all necessary information;

3.5.3. Identify the needs of supply of medical devices and consumables.

Section II

Organisational structures, activities and human resources

1. Organisational structures, basic characteristics

The organisational structures in which transfusion haematology operations are carried out are:

1.1. Blood transfusion establishments

1.2. The Military Medical Academy

1.3. (Amended SG, Issue 92 of 2010) Hospitals for active treatment whose structure includes a blood transfusion ward

1.4. Inpatient healthcare facilities with a blood transfusion laboratory (BTL)

1.5. (Amended SG, Issue 92 of 2010) Inpatient healthcare facilities without a BTL;

1.6. Laboratories at Diagnostic and Consultation Centres (DCC) and independent medical diagnostic laboratories providing immuno-haematologic testing of patients.

2. Main activities

All activities related to transfusion haematology should be carried out in strict compliance with the rules for good laboratory practice and good manufacturing practice. The main activities are regulated by the BBDBTA and the Guidelines on the Structure and Operation of the Blood Transfusion Establishments (SG, Issue 89 of 2000) and include the following:

2.1. The following activities are carried out at BTEs:

2.1.1. Planning of the supplies of blood and blood components necessary to satisfy the medical needs of healthcare facilities in the specific area and for manufacturing medicinal products from plasma;

2.1.2. Planning of medical devices for collection and storage of blood and blood components for healthcare facilities in the specific area, and in vitro diagnostic devices for the needs of the establishment;

2.1.3. Promotion, organisation, recruitment and retention of blood donors;

2.1.4. Selection of donors and collection of blood and blood components;

2.1.5. Processing of collected blood;

2.1.6. Immuno-haematologic testing of each unit of collected blood and blood products;

2.1.7. Testing of each unit of donated blood and blood products for transmissible infections;

2.1.8. Process validation;

2.1.9. Storage, issuing and distribution of blood and blood components;

2.1.10. Maintenance of a blood product pool;

2.1.11. Immuno-haematologic testing of patients and selection of blood components for each individual patient;

2.1.12. Optimal use of blood components;

2.1.13. Quality control;

2.1.14. Quality control of the activities carried out at BTEs;

2.1.15. Creation and maintenance of a second-level registry in compliance with the requirements of Regulation No. 29 of 2004 on the requirements and procedures for compilation, processing, storage and provision of information from the registry, under Article 36 of BBDBTA and the documentation forms (SG, Issue 82 of 2004) (Regulation No. 29 of 2004);

2.1.16. Provision of expert systematic counselling and aid in relation to the transfusion haematology activities regulated by BBDBTA

2.1.17. Training of the personnel employed at BTEs and BTWs in the respective area;

2.1.18. Haemovigilance

2.2. Apart from the activities under point 2.1 of Section II, the National Haematology and Transfusiology Centre (NHTC) carries out the following activities:

2.2.1. Research and applied activities in the field of transfusion haematology;

2.2.2. Activities related to the development of a national policy on transfusion haematology;

2.2.3. Expert, control, reference and consulting activities in the field of transfusion haematology;

2.2.4. Organisation of external control of the qualification of personnel at the immuno-haematologic laboratories in the country and the laboratories providing immuno-haematologic services to patients;

2.2.5. Training of healthcare professionals, healthcare specialists and biologists from all over the country in the field of transfusion haematology;

2.2.6. Systematic management of the operations of BTEs;

2.2.7. Creation and maintenance of first-level and second-level registries;

2.2.8. Planning under Article 26 of the BBDBTA.

2.3. (Amended in SG, Issue 92 of 2010) Hospitals for active treatment which have a BTW carry out the following activities:

Hospital structure of second-level expertise:

2.3.1. Promotion, organisation, recruitment and retention of blood donors;

2.3.2. Storage and issuing of blood components;

2.3.3. Immuno-haematologic testing of patients and selection of blood and blood components for each individual patient;

Hospital structure of third-level expertise:

2.3.4. Planning of the supplies of blood and blood components necessary to satisfy the medical needs of healthcare facilities in the area;

2.3.5. Planning of the supplies of medical devices for collection and storage of blood and blood components necessary for healthcare facilities in the area, and the in vitro diagnostic devices for the needs of the ward;

2.3.6. Promotion, organisation, recruitment and retention of blood donors;

2.3.7. Selection of donors and collection of blood and blood components;

2.3.8. Process validation;

2.3.9. Storage and distribution of blood components;

2.3.10. Maintenance of a blood component pool;

2.3.11. Immuno-haematologic testing of patients and selection of blood and blood components for each individual patient;

2.3.12. Quality control;

2.3.13. Quality control of the activities carried out at the ward;

2.3.14. Creation and maintenance of a third-level registry in compliance with the requirements of Regulation No. 29 of 2004;

2.3.15. Counselling related to the use of the blood and blood components in the structures of the respective hospital and the respective area;

2.3.16. Training of the personnel employed at the BTW and the employees of the other hospital wards involved in the clinical use of blood and blood components;

2.3.17. Haemovigilance.

2.4. The following activities are carried out at inpatient healthcare facilities with a blood transfusion laboratory:

2.4.1. Promotion of voluntary and non-remunerated blood donation;

2.4.2. Immuno-haematologic testing of patients and selection of blood and blood components for each individual patient;

2.4.3. Storage of blood and blood components;

2.4.4. Counselling related to the use of the blood and blood components of the structures of the respective hospital;

2.4.5. Haemovigilance;

2.4.6. Blood transfusion laboratories cannot carry out activities related to selection of donors, blood donation and blood collection as specified in Article 6, paragraph 1 of BBDBTA; collection of blood in these laboratories is carried out only for the needs of the immuno-haematologic testing of the patients of the healthcare facility.

2.5. (Amended SG Issue 92 of 2010) Inpatient healthcare facilities without a blood transfusion laboratory carry out the following activities:

2.5.1. Transfusion of blood and blood components;

2.5.2. Haemovigilance

2.6. Laboratories at Diagnostic and Consultation Centres and independent medical diagnostic laboratories carry out immuno-haematologic testing of patients and pregnant women.

3. Structure of BTEs and BTWs at hospitals for active treatment

3.1. The structure of a BTE always includes the following administrative and/or functional units for:

3.1.1. Quality management and control of blood and blood components;

3.1.2. Promotion and organisation of blood donation;

3.1.3. (Amended SG Issue 92 of 2010) Blood donation carried out by stationary or mobile teams;

3.1.4. Blood processing;

3.1.5. Blood and blood component testing;

3.1.6. Storage, issuing and distribution of blood and blood components;

3.1.7. Clinical transfusiology and immuno-haematologic testing of patients;

3.1.8. Administrative, economic and financial unit.

3.2. Apart from the activities listed in 3.1, the structure of the NHTC includes also:

3.2.1. A unit for monitoring, analysis, organisation and information support of the blood transfusion system of the Republic of Bulgaria;

3.2.2. Manufacturing units for the production of medicines from plasma and in vitro medical devices from blood.

3.3. (Amended SG Issue 92 of 2010) All BTWs carry out activities related to:

3.3.1. Promotion and organisation of non-remunerated and voluntary blood donation;

3.3.2. Blood donation carried out by stationary or mobile teams;

3.3.3. Clinical transfusiology and immuno-haematologic laboratory;

3.3.4. Storage and issuing.

4. Human resources – they depend on the scope of the activities that are carried out; the minimum requirements for the number of healthcare professionals are as follows:

4.1. Minimum requirements for the number of healthcare professionals at BTEs:

Physicians 15

Nurses 14

Medical laboratory technicians 14

4.2. (Amended SG Issue 92 of 2010) Minimum requirements for the number of healthcare professionals at BTWs:

Physicians: Specialists at first-level expertise structures: 1

Physicians of which one is a specialist: Second-level expertise structures: 2

Nurses: 4

Medical laboratory technicians: 5

4.3. (Repealed SG Issue 37 of 2007)

4.4. (Repealed SG Issue 37 of 2007)

Section III

Basic characteristics of the locations where transfusion haematology can be practised

I. Basic healthcare requirements for transfusion haematology at the different levels

1. General provisions

1.1. Location of the premises where transfusion haematology activities are carried out: ground level (Level 0) or above ground level (Level 0+).

1.2. Minimum lighted height of the premises: 2.50 m.

1.3. Walls:

1.3.1. the walls of the premises where the donated blood, blood components and blood samples are tested and processed and those of the service and sanitary premises should be

covered with materials allowing wet cleaning and disinfection on a daily basis (smooth faience, terracotta, etc.), up to at least 1.80 m from the floor in its finished state;

1.3.2. The walls of the rest of the premises and the corridors should be covered in latex paint or other coatings which allow wet cleaning and disinfection;

1.3.3. Rough plaster is not allowed on walls;

1.3.4. Oil paint is not allowed on walls.

1.4. Flooring:

1.4.1. Floorings in the premises where blood, blood components and blood samples are tested and processed, should be waterproof, resistant to thermal and chemical impact, without joints and allowing wet cleaning and disinfection on a daily basis;

1.4.2. The floorings in the service and sanitary premises should be waterproof and should allow wet cleaning and disinfection;

1.4.3. The floorings in the rest of the premises and in the corridors should allow wet cleaning and disinfection;

1.4.4. No textile floorings are allowed.

1.5. Lighting in the different types of premises should comply with the requirements of BS 1786-84 'Lighting. Natural and Artificial'.

There should be emergency lighting in all corridors and major premises. The only premises without natural lighting can be the hardware units, storage areas, service and sanitary premises.

1.6. The heating, ventilation and air-conditioning systems should comply with the Standards for design of heating, ventilation and air-conditioning systems (published in Issues 6, 7, 8 and 9 of 1986 of the Building and Architecture Bulletin (BAB).

1.7. The heating systems should ensure:

1.7.1. In premises: a minimum temperature of 18°C;

1.7.2. In corridors: 15°C.

1.8. Air-conditioning systems limiting the maximum temperature to 20 - 24 °C should be in place:

1.8.1. In the premises where people donate blood and blood components;

1.8.2. In the premises where blood samples are tested;

1.8.3. In the premises where donated blood and blood components are processed;

1.8.4. In the premises where there are more than 3 refrigeration units.

1.9. Mechanical ventilation should be in place:

1.9.1. In the premises where blood samples are tested and natural aeration is not acceptable;

1.9.2. In all other premises which cannot be naturally aerated.

1.10. Power supply and electrical systems should be designed in compliance with:

1.10.1. The guidelines for design of electrical systems (published in *Equipment*, 1980; Amended and expanded BAB, Issue 3 of 1982);

1.10.2. Regulation No. 2 on electrical systems in buildings (SG Issue 11 of 1999).

1.11. A backup power source should provide heavy-current power for:

1.11.1. All workstations of the computerised information system;

1.11.2. All refrigeration units;

1.11.3. All manufacturing facilities;

1.11.4. All laboratory equipment.

1.12. Communications:

1.12.1. between NHTC, RHTC and BTWs should be supported by an external network of a computerised information system;

1.12.2. between all workstations of the office/ward/centre and the clinics and wards to which services are provided should be supported by telephone landlines;

1.12.3. between the motor vehicles should be supported by mobile telephones;

1.12.4. with personnel on duty should be supported by pager devices and mobile telephones.

1.13. The water supply and sewage systems should be designed in compliance with the standards for design of water supply and sewage systems in buildings (published in Issues 5 and 6 of 1986 of BAB; Amended BAB, Issue 8 of 1987; Amended and expanded BAB Issue 11 of 1988 ; Promulgated SG Issue of 1995 and Issue 15 of 1996).

1.14. Sinks with running cold and hot water (from 8 to 80 °C), complying with the requirements of BS 2823-83 ‘Potable Water’, should be in place in all work premises, and service and sanitary premises.

Disinfection materials should be in place at the sinks of all laboratories and the premises where blood donation takes place, and where donated blood is processed.

Absence of sinks with running hot and cold water is only acceptable in hardware units and storage areas.

1.15. Floor drains should be in place only in service and sanitary premises.

1.16. Furniture and medical equipment surface should allow wet cleaning and disinfection.

1.17. Collection and temporary storage of household and hazardous waste from healthcare activities should be performed separately at designated locations. After the collection of hazardous waste from healthcare activities, they it be decontaminated and packed in accordance with the Waste Management Act (SG Issue 86 of 2003). The final treatment of hazardous waste (incineration) should be carried out in an in-house facility (incinerator) or by a licensed company as agreed in a dedicated contract.

1.18. Laundering of covers and work clothes should be done separately in washing machines designed for the purpose.

1.19. The general principles of asepsis and antisepsis specified in Regulation No. 2 of 2005 on the organization of prevention and control of hospital-acquired infections (SG Issue 8 of 2005) should be observed in transfusion haematology.

1.20. Disinfection and sterilization in transfusion haematology should be carried out in accordance with:

1.20.1. Guideline No. 2 of 2 September 1998 of the Ministry of Health on the procedures for disinfection in healthcare facilities (Official Bulletin of the Ministry of Health, Issue 1 of 1999);

1.20.2. Hygiene standards and requirements for conducting sterilization in the medical practice, approved by Order No. РД-09-300 of 2 July 1998 of the Minister of Health (MoH Official Bulletin No. 7 of 1999).

1.21. Access control should preclude unauthorized access to the premises. Access control should define:

1.21.1. Access time;

1.21.2. Employees and the clothing and shoes that they can wear and work with;

1.21.3. Registration of unathorised visitors (on paper or electronically).

1.22. Access control should be provided by:

1.22.1. Physical and/or technical security (alarm systems and/or video surveillance) of the building in which transfusion haematology activities are carried out;

1.22.2. Fire signalling (FSE) and fire fighting equipment (FFA).

2. Blood transfusion establishments

2.1. Required premises

2.1.1. Key premises of the Quality Management and Quality Control Unit:

2.1.1.1. Laboratory for quality monitoring (min. area 18 m^2).

2.1.1.2. Laboratory for quality control (min. area 20 m^2).

2.1.2. Main premises of the unit for promotion and organization of blood donation:

2.1.2.1. Promotion and Organization Office (min. area 12 m^2).

2.1.3. Main premises of the Donation Unit:

2.1.3.1. Registration desk for donors and reception area for blood samples from patients (min. area 12 m^2) – preferably in separate rooms;

2.1.3.2. Clinical laboratory for blood donors (min. area 12 m^2);

2.1.3.3. Medical certification office (min. area 9 m^2) for blood donors and patients under an autologous transfusion programme with preoperative collection of blood;

2.1.3.4. Blood collection office including the autologous transfusion programmes (min. area of 18 m^2);

2.1.3.5. Mobile teams blood collection office (min. area 12 m^2);

2.1.3.6. Waiting room for blood donors (min. area 12 m^2);

2.1.3.7. Blood collection materials storage area (min. area of 20 m^2);

2.1.3.8. Storage area for energising foods for blood donors (min. area of 6 m^2).

2.1.4. Main premises of the Blood and Blood Components Testing Unit:

2.1.4.1. Laboratory for immuno-haematologic testing of donated blood (min. area 20 m^2);

2.1.4.2. Laboratory for screening of each unit of donated blood for markers of transmissible infections (min. area of 20 m^2);

2.1.4.3. Quarantine laboratory materials storage area (min. area 18 m^2);

2.1.4.4. Released laboratory materials storage area (min. area 18 m^2);

2.1.4.5. Biotech unit (min. area 12 m^2).

2.1.5. Main premises of the Blood Processing Unit:

2.1.5.1. Area for acceptance of donated blood and blood components (min. area 15 m^2);

2.1.5.2. Blood and blood components processing area (min. area 25 m^2);

2.1.5.3. Blood and blood components quarantine area (min. area 15 m^2);

2.1.5.4. Labelling and release of final blood components area (min. area 15 m^2);

2.1.5.5. Storage of labelled blood and blood components for issuing to the Issuing Unit, BTWs, KKs and drug manufacturers (min. area 20 m^2);

2.1.5.6. Walk-in refrigeration unit with temperature from 2°C to 6 °C (min. area 18 m^2);

2.1.5.7. Walk-in refrigeration unit with temperatures to -30°C (min. area 18 m^2).

2.1.6. Main premises of the unit for Storage, Issuing and Distribution of Blood and Blood Components:

2.1.6.1. Immuno-haematologic laboratory for patients (min. area 20 m^2);

2.1.6.2. Labelled Blood Components facility and issuing for patients (min. size 18 m^2).

2.2. Auxiliary facilities in the establishment related to the quality of blood components:

2.2.1. Server room;

2.2.2. Sterilization of clean materials and distillation area (min. area 18 m^2);

2.2.3. Area for hazardous waste autoclaving (min. area 18 m^2);

2.2.4. Training premises;

2.2.5. Archive.

3. Blood transfusion ward at a regional hospital for active treatment

3.1. Required premises:

3.1.1. (Amended SG Issue 92 of 2010) Main donation premises:

3.1.1.1. Medical certification office (min. area 9 m^2) for blood donors and patients under an autologous transfusion programme with preoperative collection of blood;

3.1.1.2. Blood collection office including the autologous transfusion programmes (min. area of 12 m^2);

3.1.1.3. Mobile teams blood collection office (min. area 12 m^2);

3.1.1.4. Storage area for collected blood units and their satellites (min. area 10 m^2);

3.1.2. (Amended SG Issue 92 of 2010) Main premises for Clinical Transfusion and Immuno-Haematologic Laboratory:

3.1.2.1. Immuno-haematologic laboratory for patients (min. area 15 m^2);

3.1.2.2. Labelled Blood and Blood Components facility and issuing for patients (min. size 9 m^2).

3.1.2.3 Biotech unit for storage of blood samples from patients;

3.2. Auxiliary facilities of the BTW related to the quality of blood components:

3.2.1. Registration and reception desk (min. area 9 m^2) for blood samples from patients and final blood components;

3.2.2. Blood collection materials storage area (min. area 4 m^2);

3.2.3. Storage area for energising foods for blood donors (min. area of 4 m^2);

3.2.4. Laboratory materials storage area;

4. Blood transfusion laboratory at a healthcare facility:

4.1. Required premises:

4.1.1. Immuno-haematologic laboratory (min. area 15 m^2);

4.1.2. Labelled Blood and Blood Components facility (min. area 9 m^2).

4.1.3. Issuing for patients (min. area 9 m^2);

4.1.4. Registration and reception desk (min. area 9 m^2) for blood samples from patients and final blood components;

4.1.5. Laboratory materials storage area;

4.1.6. Biotech unit for storage of blood samples from patients;

II. Basic requirements for the equipment and medical devices in Transfusion Haematology at the different levels

1. General provisions

1.1. Technological equipment is selected and delivered according to material logistics plans for the activities in Transfusion Haematology:

1.1.1. The following should be in place for each unit of equipment:

1.1.1.1. Expert assessment of its compatibility with the other components and the established European standards, including quality parameters and their share in the complex assessment of the selected unit;

1.1.1.2. Specifications based on expert opinion.

1.1.2. The supplied equipment should comply with the specifications approved by experts.

1.1.3. Each unit of equipment should be accompanied by a certificate of quality.

1.1.4. Each unit of equipment should have a passport containing:

1.1.4.1. Manufacturer’s marking;

1.1.4.2. Manufacturing date;

1.1.4.3. Instructions for safe operation;

1.1.4.4. Classification of the device in accordance with the standards for medical devices (MedGV);

1.1.4.5. Definition of the unit;

1.1.4.6. Warranty period of the product and warranty rules;

1.1.4.7. Technical data, including capacity, dimensions, weight and requirements for the microclimate (temperature, humidity and air velocity);

1.1.4.8. Protection systems and mandatory inspections of protection systems;

1.1.4.9. Possible failures, analysis algorithm and approach;

1.1.4.10. Possible emergencies and instructions on how to act;

1.1.4.11. Installation rules, including transportation, installation and commissioning;

1.1.4.12. Maintenance rules, including cleaning, disinfection and technical maintenance;

1.1.4.13. Consumables (if used) and commercial substitutability range;

1.1.4.14. Setup, adjustment and checks;

1.1.4.15. Process management;

1.1.4.16. Research and experimentation results, and operational reliability;

1.1.4.17. Reproducible results under standard operating conditions;

1.1.4.18. Complete details for validation of the device by the manufacturer;

1.1.4.19. Out-of-warranty service rules;

1.1.4.20. Electrical engineering characteristics, including power supply (voltage, frequency, current, fuses), method of connecting to the mains, power consumption, applied electric security standards, compliance with technical safety rules, security test results, options for displaying parameters important for the operation of the device and their recording on paper or electronically;

1.1.4.21. Characteristics of the installed automats, including automatic error and damage detection; communications and instructions on how to act; device software and software-compatible operating systems; options of the software to work in a local network; a set of work programs; programme selection guide; procedures for process programming; displayed image format; report (protocol) management options; options for exporting information by a thermal and laser printer; data exchange options; options for archiving or real-time recording via a local computer network.

1.1.5. The main technological equipment at the BTE should be duplicated (regardless of its capacity) to maximize the automation of critical operations for compliance with the best practices:

1.1.5.1. Immuno-haematologic automatic analyzer;

1.1.5.2. Automatic analyzer for transmissible infections marker screening;

1.1.5.3. Automatic separator for donated blood;

1.1.5.4. Shock freezer;

1.1.5.5. Server.

2. Equipment identification.

2.1. Each unit of equipment performing a series of procedures (more than 1) should have a unique identification number that is recorded in its report (protocol) to finalize its work.

2.2. In case of deviations from the standard at a particular stage of the technological process, a unique identification number should be assigned to all uniform equipment that could be related to the deviations in the quality of the results / product.

3. Technological equipment control.

3.1. Each unit of equipment should have a logbook (dated and sanctioned by the operators' signatures) which contains records of the following:

3.1.1. Delivery;

3.1.2. Installation;

3.1.3. Preparation for operation;

3.1.4. Initial setup, regulation, inspection and validation;

3.1.5. Personalised technical support;

3.1.6. Personalised preventive measures;

3.2. The logbook of each instrument should contain the observations made under the individual program for quality control. These observations should be described, dated, and sanctioned by the operators' signatures):

3.2.1. Ongoing checks of settings and method adjustment;

3.2.2. Ongoing checks of the reproducibility of the results of the work and the criteria that are used (specifications, reference and working standards, etc.)

3.2.3. Faults, errors and deviations in settings and reproducibility of results, and corrective measures:

3.2.3.1. On-site repairs or services at repair centres;

3.2.3.2. Settings, adjustment, inspection and validation after repairs or maintenance;

3.2.3.3. Acceptance criteria after repair, maintenance or readjustment of devices.

3.3. Equipment for storing blood, blood components, blood samples and laboratory reagents.

3.3.1. Each unit of the group (freezer, refrigerator, platelet incubator):

3.3.1.1. should have capacity with optimal storage conditions;

3.3.1.2. should have a device that provides equal temperature values in all points of the storage space;

3.3.1.3. should be equipped with a visible thermometer;

3.3.1.4. should maintain the set temperature;

3.3.1.5. should have an alarm system that is activated in case of temperature deviations ≥ ±2°C;

3.3.1.6. should have documented rules for the measures to be undertaken by the staff in case of damage to the recording device or in case an alarm gets activated.

3.3.2. Each freezer, refrigerator and platelet incubator for storage of blood, blood components and blood samples should record continuously temperature levels either on paper or electronically.

3.3.3. Each platelet incubator should maintain the predefined shaking frequency.

3.4. Equipment for separation of blood, blood components, and blood samples, and of erythrocytes with a wash solution.

3.4.1. Each separation unit (automatic separator of blood and blood components; separator centrifuge for bags with donated blood; laboratory centrifuge; automatic washing centrifuge for antiglobulin testing):

3.4.1.1. should be equipped with a tachometer and a clock to control the acceleration, speed and stopping;

3.4.1.2. should ensure the input parameters, including acceleration, speed and stopping;

3.4.1.3. should automatically detect errors and failures and report details about them;

3.4.1.4. should have an alarm system that is activated by automatic detection of errors and failures;

3.4.1.5. should have documented rules for the measures to be undertaken by the staff in case an alarm gets activated.

3.4.2. Each separation centrifuge for bags with donated blood and blood products:

3.4.2.1. should have a visible thermometer;

3.4.2.2. should maintain the set temperature.

3.5. Blood, blood components and blood samples warmer device.

Each unit of the group (i.e. the electric coil which heats the blood flowing through the tubing of the transfusion system; the water bath; the incubator):

3.5.1. should be equipped with a visible thermometer;

3.5.2. should maintain the set temperature;

3.5.3. should have an alarm system that is activated in case of temperature deviations of 1°C;

3.5.4. should have documented rules for the measures to be undertaken by the staff in case an alarm gets activated.

Section IV

General requirements for the activities regulated by the Blood, Blood Donation and Blood Transfusion Act

I. Requirements for donor selection and blood collection

1. Donor selection

The process of selection of donors should determine whether a person is in good health, in order to protect his/her own health and to protect the recipient from transmittable diseases or medications that could harm him/her. The following selection procedures should be followed:

1.1. Verification of the information recorded in the system by personal codes to check for any previous instances of blood collection, test results, blood group and transmissible infections. In case of deviations in previous collections of blood or blood components, the donor should be excluded.

1.2. All prospective donors should be given written or oral information understandable for the general public about:

1.2.1. the essential nature of blood, the blood donation procedure, the components derived from whole blood and aphaeresis donations, and the important benefits to patients;

1.2.2. the reasons for requiring an examination, health and medical history, and the testing of donations and the significance of ‘informed consent’ (for allogeneic and autologous donations);

1.2.3. the possibility of self-deferral, and temporary or permanent deferral, and the reasons why individuals are not to donate blood or blood components if there could be a risk for the recipient (for allogeneic donations);

1.2.4. the possibility of deferral and the reasons why the donation procedure would not take place in the presence of a health risk to the individual whether as donor or recipient of the autologous blood or blood components (for allogeneic donations)

1.2.5. the reasons why individuals are not to make donations which may be detrimental to their health;

1.2.6. specific information on the nature of the procedures involved either in the allogeneic or autologous donation process and their respective associated risks; for autologous donations, the possibility that the autologous blood and blood components may not suffice for the intended transfusion requirements;

1.2.7. information on the option for the donors to change their mind prior to proceeding further, or the possibility of withdrawing or self-deferring at any time during the donation process, without any undue embarrassment or discomfort;

1.2.8. the reasons why it is important that donors inform the blood establishment of any subsequent event that may render any prior donation unsuitable for transfusion;

1.2.9. information on the responsibility of the blood establishment to inform the donor, through an appropriate meachnism, if the results show abnormality of significance to the donor's health;

1.2.10. information why unused autologous blood and blood components will be discarded and not be transfused to other patients;

1.2.11. information that the test results of detecting markers for viruses, such as HIV, HBV, HCV or other relevant blood transmissible microbiologic agents will result in donor deferral and destruction of the collected unit;

1.2.12. information on the opportunity for donors to ask questions at any time;

1.2.13. the need for donors engaged in professional or amateur dangerous activities (airplane piloting, bus or train driving, working with cranes, ladders or scaffolds climbing, paragliding, climbing or diving) to wait for at least 12h before they resume their usual activities.

1.3. Prospective donors should provide the following information:

1.3.1. Donor’s personal details which specifically and unambiguously identify the donor, as well as contact details;

1.3.2. health and medical history provided on a questionnaire and through a personal interview performed by a qualified healthcare professional, that includes relevant factors that may assist in identifying and screening out persons whose donation may present a health risk to others, such as the possibility of transmitting diseases, or health risks to themselves.

1.4. The donor should sign the donor questionnaire and this signature certifies that:

1.4.1. he/she has read and understood the information that has been provided to him/her;

1.4.2. he/she has had the opportunity to ask questions;

1.4.3. he/she has been provided with satisfactory responses to any questions asked;

1.4.4. he/she has given an informed consent in writing to proceed with the donation process;

1.4.5. he/she has been informed, in the case of autologous blood donations, that the donated blood and blood components may not be sufficient for the expected transfusion requirements; and

1.4.6. he/she acknowledges that the information provided by him/her is correct to the best of his/her knowledge.

1.5. The questionnaire should also be signed by the medical staff responsible for drawing up a report on the medical history of the donor.

1.6. The completed declaration, the informed consent and the blood donation card should be reviewed in the presence of the donor.

1.7. A physical examination should be performed including:

1.7.1. Appearance assessment;

1.7.2. General health condition assessment;

1.7.3. Measurement of:

1.7.3.1. blood pressure - systolic pressure should not exceed 180 mm Hg and diastolic pressure should not exceed 100 mm of mercury column;

1.7.3.2. pulse – acceptable values range from 60 to 100 beats per minute;

1.7.3.3. temperature – it should not exceed 37°C;

1.7.4. others, at the discretion of the physician in the blood collection team.

1.8. The donor’s blood type should be determined and haemoglobin levels measured.

1.9. The selection of donors of whole blood and blood components should comply with the following criteria:

1.9.1. Selection criteria for donors of whole blood and blood components.

In exceptional circumstances, individual donations from donors who do not meet the following criteria may be authorized by a qualified healthcare professional. All such cases should be clearly documented.

The following criteria do not apply to autologous donations.

1.9.1.1. Age and body weight of donors

Age	18 to 65 years	
	First-time donor over 60 years	At the discretion of the healthcare professional
Body weight	>= 50 kg for donors of whole blood or aphaeresis blood components	

1.9.1.2. Haemoglobin levels in donor's blood

Haemoglobin	For females >= 125 g/l	For males >= 135 g/l	Applicable to allogeneic donors of whole blood and blood components

1.9.1.3. Protein levels in donor's blood

Protein	>= 60 g/l	The protein analysis for aphaeresis plasma donations must be performed at least annually

1.9.1.4. Platelet levels in donor's blood

Platelets	Platelet number	Level required for aphaeresis platelet donors

	greater than or equal to 150 x 10(9)/l	

1.9.2. Deferral criteria for donors of whole blood and blood components

The tests and deferral periods marked by an asterisk (*) are not required when the donation is used exclusively for plasma for fractionation.

1.9.2.1. Permanent deferral criteria for donors of allogeneic donations

Cardiovascular disease	Prospective donors with active or past serious cardiovascular disease, except congenital abnormalities with complete cure
Central nervous system disease	A history of serious CNS disease
Abnormal bleeding tendency	Prospective donors who give a history of coagulopathy
Repeated episodes of syncope, or a history of convulsions	Other than childhood convulsions or where at least 3 years have elapsed since the date the donor last took anticonvulsant medication without any recurrence of convulsions
Gastrointestinal, genitourinary, haematological, immunological, metabolic, renal, or respiratory system diseases	Prospective donors with serious active, chronic, or relapsing disease
Diabetes	If being treated with insulin
Infectious diseases	Hepatitis B, except for HBsAg-negative persons who are demonstrated to be immune
	Hepatitis C
	HIV-1/2

	HTLV I/II
	Babesiosis *
	Kala-azar (visceral leishmaniasis) (*)
	Trypanosomiasis cruzi (Chagas' disease) (*)
Malignant diseases	Except in situ cancer with complete recovery
Transmissible spongiform encephalopathis (TSEs) (e.g. Creutzfeldt Jacob Disease, variant Creutzfeldt Jacob)	Persons who have a family history which places them at risk of developing a TSE, or persons who have received a corneal or dura mater graft, or who have been treated in the past with medicines made from human pituitary glands. For variant Creutzfeldt Jacob disease, further precautionary measures may be recommended.
Intravenous (IV) or intramuscular (IM) drug use	Any history of non-prescribed IV or IM drug use, including bodybuilding steroids or hormones
Xenotransplant recipients	
Sexual behaviour	Persons whose sexual behaviour puts them at high risks of acquiring severe infectious diseases that can be transmitted by blood

1.9.2.2. Temporary deferral criteria for donors of allogeneic donations.

1.9.2.2.1. Infections

Duration of deferral period

After an infectious illness prospective donors shall be deferred for at least 2 weeks following the date of full clinical recovery.

However, the following deferral periods shall apply for the infections listed in the table:

Brucellosis (*)	2 years following the date of full recovery
Osteomyelitis	2 years after confirmed cured
Q fever (*)	2 years following the date of confirmed cured

Syphilis (*)	1 year following the date of confirmed cured
Toxoplasmosis (*)	6 months following the date of clinical recovery
Tuberculosis	2 years following the date of confirmed cured
Rheumatic fever	2 years following the date of cessation of symptoms, unless evidence of chronic heart disease
Fever > °C	2 weeks following the date of cessation of symptoms
Flu-like illness	2 weeks after cessation of symptoms
Malaria(*)	
- Individuals who have lived in a malarial area for 6 months in a row in any given period of their life	May be accepted as blood donors if the result of a validated immunological test for antibodies to the malaria parasite taken at least 4 months after last visit to a malaria-endemic area is negative. If the test result is positive, the donor is excluded from donation for good. If not test has been conducted, the donor is excluded from donation for good.
- Individuals with a history of malaria	3 years following cessation of treatment and absence of symptoms. Accept thereafter only if an immunologic or molecular genomic test is negative
- Asymptomatic visitors to endemic areas	6 months after leaving the endemic area unless an immunologic or molecular genomic test is negative;
- Individuals with a history of undiagnosed febrile illness during or within 6 months of a visit to an endemic area	3 years following resolution of symptoms; may be reduced to 4 months if an immunologic or molecular test is negative

West Nile Virus (WNV) (*): 28 days after leaving an area with ongoing transmission of WNV to humans.

1.9.2.2.2. Exposure to risk of acquiring a transfusion-transmissible infection

- Endoscopic examination using flexible instruments - Mucosal splash with blood or needlestick injury - Transfusion of blood components - Tissue or cell transplant of human origin - Major surgery - Tattoo or body piercing - Acupuncture unless performed by a qualified practitioner and with sterile single-use needles - Persons at risk due to close household contact with persons with hepatitis B	Defer for 6 months, or for 4 months provided a NAT test for hepatitis C is negative
Persons whose behaviour or activity places them at risk of acquiring infectious diseases that may be transmitted by blood	Defer after cessation of risk behaviour for a period determined by the disease in question, and by the availability of appropriate tests

1.9.2.2.3. Vaccination

Attenuated viruses or bacteria	4 weeks
Inactivated/killed viruses, bacteria or rickettsiae	No deferral if well
Toxoids	No deferral if well

Hepatitis Aor hepatitis B vaccines	No deferral if well and if no exposure
Rabies	No deferral if well and if no exposure. If vaccination is given following exposure defer for 1 year
Tick-borne encephalitis vaccines	No deferral if well and if no exposure

1.9.2.2.4. Other temporary deferrals

Pregnancy	6 months after delivery or termination, except in exceptional circumstances and at the discretion of a physician
Minor surgery	1 week
Dental treatment	Minor treatment by dentist or dental hygienist: defer until next day (NB: Tooth extraction, root-filling and similar treatment is considered as minor surgery).
Medication	Based on the nature of the prescribed medicine, its mode of action and the disease being treated

1.9.2.3. Deferral for particular epidemiological situations

Particular epidemiological situations (e.g. disease outbreaks)	Deferral consistent with the epidemiological situation (These deferrals should be notified by the competent authority to the European Commission with a view to Community action)

1.9.2.4. Deferral criteria for donors of autologous donations

Serious cardiac disease	Depending on the clinical setting of the

	blood collection
Persons with or with a history of: - hepatitis B, except for HBsAg-negative persons who are demonstrated to be immune - hepatitis C - HIV-1/2 - HTVL I/II	Healthcare facilities establish specific provisions for autologous donations by such persons
Active bacterial infection	

1.10. Additional requirements for aphaeresis blood component donors

1.10.1. Aphaeresis blood component donors should meet all the requirements set for whole blood donors.

1.10.2. Prospective aphaeresis donors cannot be individuals with:

1.10.2.1. abnormal bleeding;

1.10.2.2. fluid retention (particularly if this implies the application of corticosteroids, and/or using plasma substitutes);

1.10.2.3. use of medication containing acetyl salicylic acid during the last 5 days before platelet aphaeresis;

1.10.2.4. stomach disorders (If corticosteroids are used);

1.10.2.5. adverse reactions during previous collections of blood components.

After selection, prospective donors should be referred for blood or blood components collection.

2. (Amended SG Issue 37, 2007) Blood collection. Collection of blood or blood components can be commenced only after all procedures and tests provided for in this standard are carried out and a medical examination is performed by a healthcare professional. Blood collection should be carried out in systems of sterile bags with CE markings in accordance with the requirements of Directive 98/79/EC. Blood should be taken at stationary BTEs, hospitals for active treatment with BTWs and by mobile teams at such hospitals.

2.1. Blood collection should be performed in accordance with the standard operating protocol by a nurse trained at a blood establishment and holding a specific certificate.

2.2. (Amended SG Issue 37, 2007) The person collecting the blood or blood components should observe the following mandatory sequence of activities in the implementation of the procedure:

2.2.1. prepare a set of documents containing completed forms such as:

2.2.1.1. an informed consent;

2.2.1.2. a health certificate;

2.2.1.3. a donor card containing the results of the medical examination and laboratory tests;

2.2.1.4. a personal blood donor card (given to each donor upon first donation of blood or blood components);

2.2.1.5. identify the collected blood or blood components;

2.2.2. verify that the bags have no defects;

2.2.3. label the bags;

2.2.4. (Amended SG Issue 37 of 2007) prepare and label at least two vacutainers for satellite blood collection and identify the donor;

2.2.5. (Amended SG, Issue 37 of 2007) verify the exact correspondence of the identity of the donor and the labels placed on the bag and the vacutainer;

2.2.6. use a precise standardised procedure to prepare the site of injection and avoid touching it prior to inserting the needle into the vein;

2.2.7. perform venipuncture; the needle should puncture the vein on the first try; it is acceptable to make a second aseptic venipuncture with a new needle at a different location;

2.2.8. ensure adequate mixing of blood with anticoagulant at all blood collection stages by monitoring the following:

2.2.8.1. when the blood starts to flow, it should immediately come into contact with the blood conserving solution and get mixed well;

2.2.8.2. the blood flow should be sufficiently strong and continuous; ideally, the collection of one unit of whole blood should not last more than 10 min; if the collection of blood lasts for more than 12 min, the blood should not be used to obtain platelet concentrate; if the collection of blood lasts for more than 15 min, the plasma should not be used for transfusion or preparation of clotting factors;

2.2.8.3. if during aphaeresis the flow is interrupted, the unit should not be used for fractionation of labile plasma proteins or for preparation of platelet concentrates;

2.2.8.4. when mixing is performed manually, the bag of blood should be turned over every 30 to 45s; when automatic mixing is used, a well standardized system should be applied;

2.2.9. (Amended SG, Issue 37 of 2007) monitor the amount of blood in the bag, and cease blood collection when the standard volume of a single donation unit is reached;

2.2.10. (Amended SG Issue 37 of 2007) collect blood in pre-labelled vacutainers as specified in point 2.2.4 directly from the bloodletting system, using an adapter;

2.2.11. (Amended SG, Issue 37 of 2007) close the tube of the full sack effectively immediately upon termination of blood collection, and advance the content of the tube into the bag;

2.2.12. (Amended SG, Issue 37 of 2007) examine the labels of the bag, the satellite blood samples and the identity of the donor to ensure label conformity;

2.2.13. store the blood unit at suitable temperature.

2.3. Each blood and blood components collection should be properly documented and should include the following details:

2.3.1. date, donation number, identification and medical history of the donor;

2.3.2. date, donation number, identification and medical history of the donor of each unsuccessful donation and the reasons for such failure;

2.3.3. list of rejected donors and reasons;

2.3.4. full details about any adverse reactions during blood donation;

2.3.5. aphaeresis donors: quantity of collected component, quantity of processed blood, quantity of substitute and quantity of anticoagulant.

2.4. Quantity of donated blood and blood components and intervals between collections:

2.4.1. Whole blood

2.4.1.1. a standard whole blood units e equals 450 ml ± 10%, without the anticoagulant;

2.4.1.2. the blood volume taken during a single donation of whole blood should not exceed 13% of the circulating blood; this quantity depends on the height and weight of the donor;

2.4.1.3. each standard blood donation includes collection of up to 45 ml in satellite sealed test tubes used to test the blood unit;

2.4.1.4. male blood donors can donate blood up to 5 times a calendar year, and women blood donors can donate blood up to 4 times a calendar year, and the interval between two donations should not be less than 60 days.

2.4.2. Aphaeresis

2.4.2.1. plasma is taken by automatic or manual plasmaphaeresis: either as a single donation or in cycles;

2.4.2.2. one plasmaphaeresis cycle includes two or more plasmaphaereses, subject to the mandatory interval of not less than 72 h that has to elapse between two cycles; the maximum quantity of plasma collected during the entire cycle should not exceed 5 l;

2.4.2.3. the mandatory interval between each plasma collection cycle is 3 months, and the total quantity of plasma collected in one year should not exceed 15 l;

2.4.2.4. in manual plasmaphaeresis, the amount of blood from which plasma is separated should not exceed 1000 ml; in such cases plasmaphaeresis is carried out at two stages of 500 ml each;

2.4.2.5. one donor can not donate more than one litre of plasma per week;

2.4.2.6. in the absence of volume substitution, not more than 650 ml of anticoagulant plasma should be taken in one aphaeresis procedure from a single donor; if the quantity collected in a single procedure exceeds 600 to 650 ml, adequate replacement of fluid loss should be insured;

2.4.2.7. loss of red blood cells should not exceed 20 ml of packed red cells per week;

2.4.2.8. the interval between a plasmaphaeresis procedure and a collection of whole blood should be at least 48 h; the interval between donation of whole blood (or unsuccessful return of separated erythrocytes in aphaeresis) and subsequent aphaeresis procedures should be at least two months;

2.4.2.9 platelet and granulocyte concentrate donation may be performed by a single cytophaeresis or in a cytophaeresis cycle; such cycle includes two consecutive cytophaereses subject to a mandatory interval of not less than 72 h that has to elapse between them;

2.4.2.10. each donor can be included in three cytophaeresis cycles over one year, when the interval between two consecutive cycles is at least two months;

2.4.2.11. when collection is carried out by automatic cytophaeresis, the quantity of blood passing through the apparatus should not exceed the quantity of the circulating blood;

2.4.2.12. the interval between collection of whole blood and collection of two units of packed red blood cells should not be less than 3 months; the interval between the aphaeresis of 2 units of packed red cells, and the collection of a single unit of whole blood should be not less than 6 months; the total annual loss from collection of packed red cells should not exceed the approved quantity for donors of whole blood;

2.4.2.13. at the discretion of the healthcare professional, it may be acceptable to take two units of packed red cells within shorter intervals in autologous aphaeresis;

2.4.2.14. in routine supply of platelet concentrates by aphaeresis, the donor should not undergo the procedure more often than once every 2 weeks; in the case of specific HLA/HPA cytophaeresis, the interval may be reduced at the discretion of the healthcare professional who is in charge of the procedure.

2.4.3. Requirements for erythrocytapheresis of two units of packed red blood cells:

2.4.3.1. the donor's blood volume should exceed 5 l;

2.4.3.2. the haemoglobin level specified before donation should exceed 140 g/l or 8.7 mmol/l (with minimum hematocrit levels above 0.42);

2.4.3.3. to ensure the donor's safety, haemoglobin levels should not be allowed to fall below 110 g/l;

2.4.3.4. in autologous aphaeresis of 2 units of packed red blood cells, lower haemoglobin levels may be allowed at the discretion of the healthcare professional.

II. Requirements for testing of donated blood

1. Immuno-haematologic testing and diagnostic markers for transmissible infections in donated blood and blood components should be performed in accordance with Regulation No. 18 of 2004 on the terms and conditions for testing, processing and storage of blood and blood components and the quality of imported blood (Regulation No. 18 of 2004).

2. Testing of donated blood and blood components for markers of transmissible infections should be performed in specialized laboratories of the National Haematology and Transfusiology Centre and the Blood Transfusion Establishments by healthcare professionals with specialisation in (or specialising in) transfusion haematology.

3. Immuno-haematologic testing of donated blood and blood components should be performed in specialized immuno-haematologic laboratories of the NHTC and BTEs by healthcare professionals with specialisation in (or specialising in) transfusion haematology.

4. Reporting and reading of results from the immuno-haematologic testing should be carried out by a healthcare professional with specialisation in or specialising in transfusion haematology, with no less than three years of continuous professional experience in a specialised immuno-haematologic laboratory.

5. Recording of blood groups using the ABO system and Rh (D) antigen is acceptable if carried out by a healthcare professional with no less than one year of professional experience in a specialised immuno-haematologic laboratory.

6. Laboratories should record the continuous training of their personnel, any staff skills testing, maintenance and calibration of equipment, control of the conditions of storage of materials and research reagents.

7. (Amended SG, Issue 37 of 2007) Donated blood screening should use only medical devices with CE marking in accordance with the requirements of Directive 98/79/EC.

8. The quality of the testing should be ensured by the following measures:

8.1. daily internal quality control of all reagents and methods; control tests should be carried out prior to batch release for sensitivity, specificity, reproducibility, etc., depending on the controlled reagents;

8.2. external quality controls, in particular confirmation of positive samples, performed by specialized NHTC laboratories;

8.3. periodic internal reviews by panels of sera or test erythrocytes prepared according to specific standards;

8.4. mandatory participation at least once a year in external skills testing organized by specialized NHTC laboratories.

9. Specialized laboratories should be actively involved in the collection and analysis of epidemiological data on the dissemination of transmissible infections at a national level as part of the haemovigilance system;

III. Requirements for the immuno-haematologic testing of patients:

1. The immuno-haematologic testing includes a set of tests aimed at determining the blood group characteristics of blood. It includes the following processes:

1.1. identification of the antigens in blood cells and blood plasma

1.2. detection of antibodies, specifically directed to the antigens of blood cells

1.3. analysis of the reactions between the antigens of blood cells and their specific antibodies.

2. Procedures used in immuno-haematologic tests have different acceptable variants. The accuracy and reliability of each variant should be established and documented in the laboratory, or should be confirmed by data published by other laboratories.

3. The minimum criteria laid down in the standard should be followed by all laboratories performing immuno-haematologic testing of patients, and may be useful for their accreditation.

4. The immuno-haematologic testing of patients should be carried out in the organizational structures specified in Section II, paragraphs 1.1, 1.2, 1.3, 1.4, 1.5.

5. Requirements for the competence to carry out immuno-haematologic testing of patients:
5.1. immuno-haematologic testing of patients should be performed by laboratory technicians, biologists or physicians meeting the requirements set out in Section I, paragraphs 3.1, 3.3, 3.4;
5.2. Reporting and reading of results from immuno-haematologic testing should be carried out by professionals as listed in Section Four, paragraph II *Requirements for diagnosis of donated blood*.

6. Basic characteristics of the places where immuno-haematologic testing of patients is carried out:
6.1. the places where immuno-haematologic testing of patients can be performed should meet the basic sanitary and technical requirements specified in Section III, section I;
6.2. basic requirements for the equipment in immuno-haematologic testing laboratories:
6.2.1. laboratories should have a sufficient number of refrigerators and freezers, which allow separate storage of specimens and test reagents; refrigerators should maintain temperatures from +2 to +8°C, and freezers -20 ° C and lower; they should be equipped with a thermometer and temperature levels should be recorded at least twice a day; temperatures should be recorded in dedicated logbooks; it is recommended that refrigerators equipped with recording thermometers and alarm systems should be used; there should also be a second thermometer in the refrigerator, independent of the recording thermometers;

6.2.2. the thermostats and water baths should be capable of maintaining temperatures from 37 to 56°C; they should be equipped with thermometers and temperature levels should be recorded at least twice a day; such readings should be recorded in a dedicated logbook; it is recommendable that they should be equipped with devices that read temperature levels constantly, as well as incubation times;

6.2.3. laboratory centrifuges should feature the following centrifugation modes:

6.2.3.1. centrifugation time: from 15 s to 5 min;

6.2.3.2. revolutions per minute: 1500 rpm to 3000 rpm.

Laboratories should be equipped with laboratory centrifuges to wash erythrocytes.

6.2.4. immersion and/or phase-contrast microscope;

6.2.5. laboratory equipment should allow regular sanitisation and disinfection;

6.2.6. the laboratory should observe, monitor and record the parameters of the equipment according to the requirements given with the manufacturer's instructions;

6.2.7. the laboratory should create conditions for preventive maintenance and calibration of all equipment.

6.3. Basic requirements for the medical equipment and supplies:

6.3.1. a sufficient number of 12-well plastic plates for blood group testing ABO and Rh D;

6.3.2. slides (or glass plates), cut at one end;

6.3.3. Pasteur pipettes and/or automatic pipettes with sizes 10, 40, 50, 100 or 1000 µl;

6.3.4 handpieces for automatic pipettes for single use;

6.3.5. tubes sized 12/75 mm (glass or transparent plastic)

6.3.6. tubes sized 16/100 mm (glass or transparent plastic);

6.3.7. stirring rods (glass, plastic or wooden);

6.3.8. containers for containers moisture chamber;

6.3.9. glass or plastic vials for dispensing saline;

6.3.10. plastic tube rack;

6.3.11. magnifier;

6.3.12. alarm clock;

6.3.13. sterile sealed containers with vacuum blood sampling (closed system for blood collection) with appropriate quantities (3.5 and 7 ml) with or without anticoagulant;

6.3.14. needles for venipuncture corresponding to the blood sample container types;

6.3.15. the material of which the medical devices are made should not react with the test reagents or samples to be tested; when they are intended for repeated use, the material should allow sanitisation and disinfection;

3.6.16. biological material (hazardous waste) containers;

6.3.17. cotton;

6.3.18. bandage;

6.3.19. disposable gloves;

6.3.20. skin disinfectant: suitable for cleaning the venipuncture site;

6.3.21. detergents and disinfectants;

3.6.22. disinfectant for floors, work surfaces, equipment and medical equipment;

6.3.23. detergents and disinfectants should be suitable for their intended purpose and should not react with the in vitro diagnostic medical devices and test samples; they should not be corrosive, irritating or allergenic.

7. The blood samples for immuno-haematologic testing of patients should meet the requirements of Regulation No. 18 of 2004.

8. In vitro diagnostic medical devices intended for immuno-haematologic testing of patients should meet the requirements of Regulation No. 18 of 2004, Article 9, Annex No. 1.

9. Analytical principles of immuno-haematologic testing of patients.

9.1. determination of blood groups of the ABO system:

9.1.1. blood groups should be determined for each patient admitted to hospital, when transfusion is a possibility during treatment;

9.1.2. blood groups should be determined for all pregnant women upon registration of their pregnancy (10-16 gestation week);

9.1.3. blood groups should be determined for all infants born to:

9.1.3.1. Rh (D) negative mothers;

9.1.3.2. mothers with clinically relevant antibodies detected during the period of pregnancy;

9.1.3.3. biological parents with ABO blood type incompatibility established during pregnancy;

9.1.4. blood groups should be determined by a cross-matching method which involves the following:

9.1.4.1. analysis of erythrocyte antigens with one set of test reagents, anti-A, anti-B and anti-A + B, or anti-AV from the same source;

9.1.4.2. analysis of anti-A and anti-B antibodies with one set of test red blood cells A_1, A_2, B and O from the same source;

9.1.4.3. determination of blood groups of newborns and children up to 6 months of age should be carried out in parallel only with test reagents anti-A, anti-B and anti-AB, derived from two sources;

9.1.4.4. in case of mismatch in the results of the tentative and final testing of the blood groups of the antigens of the ABO system, no results should be issued; a new blood sample is required the patient.

9.2. Determination of Rh (D) antigen:

9.2.1. Rh (D) antigen should be determined for all patients upon admission to hospital, when transfusion is a possibility during treatment;

9.2.2. Rh (D) antigen should be determined for all pregnant women upon registration of their pregnancy (10-16 gestation week);

9.2.3. Rh (D) antigen should be determined for all infants born to:

9.2.3.1. Rh (D) negative mothers;

9.2.3.2. mothers with clinically relevant antibodies detected during the period of pregnancy;

9.2.3.3. biological parents with ABO blood type incompatibility established during pregnancy;

9.2.4. the analysis should be performed with anti-Rh (D) reagent test:

9.2.4.1. if results are negative, the test should be repeated with anti-Rh (D) test reagent from another source;

9.2.4.2. if the negative result is confirmed, the patient is classified as Rh (D) negative.

9.3. Determination of antigen C, c, E, e of the Rhesus and Kell systems:

9.3.1. determination of C, c, E, e antigens should be carried out on patients who will be subjected to repeated transfusions; patients with thalassemia; haemogloinosis; malignant homeopathies; autoimmune haemolytic anaemia; female children; pregnant women and women of child-bearing age;

9.3.2. the analysis is carried out with monospecific anti-C, anti-c, anti-E and anti-e and anti-Kell test reagents.

9.4. analysis of erythrocyte antigens outside the ABO, Rh and Kell systems:

9.4.1. analysis of erythrocyte antigens outside the ABO, Rh and Kell systems should be carried out at the discretion of a healthcare professional specialized in transfusion

haematology; the most common are cases when a patient needs a transfusion of blood or blood components under an antigenic formula;

9.4.2. the analysis should be carried out with test reagents specific for the determination of antigens.

9.5. Analysis to search for red cell antibodies:

9.5.1. analysis to search for red cell antibodies should be performed on all patients who will undergo blood transfusion;

9.5.2. this analysis includes the following methods:

9.5.2.1. direct antiglobulin test with polyspecific antiglobulin serum;

9.5.2.2. indirect antiglobulin test with polyspecific antiglobulin serum;

9.5.2.3. agglutination and enzyme test, or other tests of equivalent sensitivity;

9.5.3. in patients with prior or future blood transfusions, the following analyses should be carried out for red cell antibody testing:

9.5.3.1. previous transfusions carried out:

9.5.3.1.1. 3 to 14 days ago;

9.5.3.1.2. 14 to 28 days ago;

9.5.3.1.3. 28 days to 3 months ago;

9.5.3.2. red cell antibodies testing of a blood sample taken:

9.5.3.2.1. 24 h prior to transfusion;

9.5.3.2.2. 72 h prior to transfusion;

9.5.3.2.3. one week prior to transfusion;

9.5.4. if the test result is positive, the specificity of red cell antibodies should be determined;

9.5.5. transfusion without testing for red cell antibodies can be performed on patients admitted due to an emergency;

9.5.6. testing for red cell antibodies should be performed on all pregnant women upon registration of their pregnancy (10-16 gestation week) and between the 28^{th} and the 34^{th} week of gestation;

9.5.7. this analysis includes the following methods:

9.5.7.1. direct antiglobulin test with polyspecific antiglobulin serum;

9.5.7.2. indirect antiglobulin test with polyspecific antiglobulin serum;

9.5.7.3. agglutination and enzyme test, or other test of equivalent sensitivity;

9.5.8. if the results from the test are positive for red cell antibodies, the following additional measures should be taken:

9.5.8.1. determination of the specificity and quantity (titre) of the antibodies;

9.5.8.2. a serum or plasma sample with a positive result of the test for red cell antibodies should be stored frozen at -20°C; in the follow-up process, it should be tested alongside the new sample;

9.5.9. if there is evidence of clinically significant red cell antibodies, follow-ups are performed:

9.5.9.1. up to 28th gestation week - every month;

9.5.9.2. from 28th gestation week until birth - every two weeks;

9.5.10. in case of blood type incompatibility between a pregnant woman and the biological father, the amount (titre) of anti-A and anti-B antibodies should be monitored; the analysis should be carried out in the period between 10th to 16th week of gestation and from 28th to 36th week of gestation; the serum or plasma samples should be stored frozen at -20°C; during the follow-up process, it should be examined alongside the new blood sample;

9.5.11. a red cell antibodies analysis should be performed for each Rh (D) negative pregnant woman in accordance with paragraph 9.5.2;

9.5.12. a red cell antibodies analysis should be performed for each pregnant woman with clinically significant antibodies established during pregnancy, in accordance with paragraph 9.5.2; if there are clinically significant red cell antibodies, their specificity and quantity (titre) should be determined;

9.5.13. a direct antiglobulin test should be performed on all newborns of Rh (D) negative mothers and mothers with clinically relevant antibodies established during pregnancy, within 72 h after birth;

9.5.14. the specificity of the red cell antibodies should be determined with a test erythrocytes panel using the method by which the antibodies were found;

9.5.15. the quantity (titre) of red cell antibodies should be determined in reducing dilutions of the tested serum (plasma) with test erythrocytes with the respective antigen in a homozygous form; the analysis is carried out using the method by which the antibodies were found.

9.6. Pre-transfusion in vitro compatibility testing:

9.6.1. each blood unit intended for transfusion should be selected according to the ABO and Rh (D) characteristics of the recipient;

9.6.2. each blood unit to be transfused should undergo pre-transfusion in vitro compatibility tests with serum (plasma) from the receiver and erythrocytes from the blood unit;

9.6.3. these in-vitro compatibility tests should include:

9.6.3.1. a quick centrifugation tube test (or agglutination test at room temperature and 37°C) and an indirect antiglobulin test;

9.6.3.2. other methods of equivalent sensitivity;

9.6.4. if there are red cell antibodies in the serum or plasma of the recipient, the blood for transfusion must be free of erythrocyte antigens targeted by the antibodies;

9.6.5. compatibility testing should be carried out independently of the negative results of the red cell antibodies testing of the receiver and the preliminary selection according to the antigenic formula of the blood for transfusion;

9.6.6. in emergency circumstances, when the life of the patient is in danger, pre-transfusion in vitro compatibility tests may only include the following:

9.6.6.1. selection of blood, according to ABO and Rh (D) characteristics of the receiver;

9.6.6.2. quick centrifugation tube test;

9.6.6.3. red cell antibodies testing should be performed immediately after transfusion of a blood sample collected from the recipient prior to transfusion.

10. Quality Control:

10.1. In order to ensure accuracy and reliability of the obtained results, each immuno-haematologic diagnostic laboratory should have an established quality assurance system. Quality control of the serological techniques should be based on:

10.1.1. an internal quality control system;

10.1.2. participation in external quality assessment systems;

10.2. Internal quality control system.

The internal quality control system validates results by monitoring the critical steps of the testing process. Internal quality control is carried out by the laboratory itself. The results of this monitoring should be documented and periodically reviewed and analysed by the head of the laboratory.

10.2.1. control of the quality of the equipment – it should be performed continuously and includes:

10.2.1.1. control of the temperature of refrigerators, freezers, thermostats and water baths;

10.2.1.2. control of the parameters of centrifuges;

10.2.1.3. control of the optical system of microscopes;

10.2.1.4. control of the parameters of the automated immuno-haematologic testing systems according to the manufacturer's instructions;

10.2.1.5. documented equipment cleaning;

10.2.1.6. documented calibration of the parameters of the equipment;

10.2.2. quality control of reagents:

10.2.2.1 reagents control should detect any deviations from the established minimum quality requirements;

10.2.2.2. the control methods that are used should conform to the methods specified by the manufacturer;

10.2.2.3. for all reagents that are prepared on site there should be clear formulas and strictly defined operational procedures;

10.2.2.4. daily control of the test reagents before the beginning of the testing process;

10.2.3. control methods:

10.2.3.1. development of written standard operating protocols for all activities in the laboratory;

10.2.3.2. inclusion of control measures in the series of tests; the number of control measures depends on the number of performed tests, but should not be less than one per day for each method used;

10.2.3.3. any change in the method of analysis must be duly validated before inclusion in the process;

10.2.4. documentation;

10.2.5. staff training;

10.2.6. error analysis and correction measures;

10.3. External quality assessment system: each laboratory should participate in an external quality assessment system in accordance with Section IV, paragraph II.

IV. Clinical use of blood and blood components

1. Requirements for homologous and autologous transfusion of blood and blood components

1.1. Each unit of blood and blood components used for clinical application should meet the requirements of Regulation No. 18 of 2004 on the terms and conditions of testing, processing and storage of blood and blood components and the quality of imported blood (SG No. 58 of 2004).

1.2. The purpose of the clinical use of blood and blood components is to:

1.2.1. support the transport of oxygen and carbon dioxide;

1.2.2. adjust homeostasis.

1.3. Transfusion of blood and blood components should be appointed by a qualified physician who should identify and list in the medical records the specific type, quantity and method of administration.

1.4. Transfusion of blood and blood components should be performed under the supervision of a qualified physician. The transfusion of blood or blood components should be carried out in strict compliance with the rights of the patient and upon obtaining an informed consent in writing from the patient, for which he/she will be provided with comprehensible information about:

1.4.1. the reasons for transfusion of blood or blood components;

1.4.2. the purpose of blood transfusion and the expected results;

1.4.3. the possible side effects and potential risks associated with the transfusion blood or blood components;

1.4.4. the alternatives to transfusion therapy and the risks associated with them.

1.5. When the patient is incapacitated, informed consent should be obtained from his/her legal representative or guardian.

1.6. Transfusion of blood or blood components without obtaining an informed consent may be performed when the life of the patient is in danger:

1.6.1. the patient’s physical or mental condition prevents him/her from giving an informed consent;

1.6.2. the patient is incapacitated and it is impossible to obtain a timely consent from his/her legal representative or guardian.

1.7. The decision and reasons specified in Section 1.6 should be recorded in the medical record of the patient by the physician who referred him/her for blood transfusion.

1.8. The patient, or his/her legal representative or guardian, may refuse transfusion of blood or blood components at any time during treatment.

1.9. Refusal under Section 1.8 should be certified by the signatures of the person and the attending physician or of the attending physician and a witness, if the patient refuses to sign it.

1.10. Transfusion of untested blood or blood components or expired blood or blood components is strictly prohibited.

1.11. Dissemination of data revealing the recipient's identity is strictly prohibited.

1.12. No drugs can be added to the blood or blood components other than saline up to 100 ml.

2. Preparation for the transfusion of blood and blood components:

2.1. Patients who are about to receive transfusion: The healthcare professional should:

2.1.1. inform the patient of the need for and benefits of the transfusion of blood or blood components (packed red cells), and of any complications which may occur;

2.1.2. obtain an informed consent in writing from the patient;

2.1.3. record any medical history related to the administration of blood and blood products in the past, and to any possible side effects and complications associated with them; any complications in prior pregnancies of female patients; register all such details in the hospital reference documentation and in the immuno-haematologic test form (Annex No. 13 to Regulation No. 29 of 2004);

2.1.4. control the collection of 5-10 ml of venous blood from the patient in a suitable container;

2.1.5. control in the presence of the patient the labelling of the blood sample which should contain the full name, personal number, hospital reference number;

2.1.6. determine the patient's blood type (ABO) in his/her presence, by test reagents anti-A, anti-B and anti-A, B and complete a immuno-haematologic test form in accordance with Annex No. 13 to Regulation No. 29 of 2004;

2.1.7. send the blood sample and completed form to an immuno-haematologic testing laboratory to confirm the blood type;

2.1.8. attach the form to the results from the immuno-haematologic testing received from the immuno-haematologic laboratory in the hospital records;

2.1.9. if there is a discrepancy between the results of the blood type tests conducted by the attending physician and the immuno-haematologic laboratory, the former should collect a new sample from the donor and repeat the entire procedure;

2.1.10. request forms for blood or blood components can be completed only by a healthcare professional, in triplicate, in accordance with Annex No. 15 to Regulation No. 29 of 2004.

3. Duties of the healthcare professional before transfusion of blood or blood components:
3.1. identify the recipient according to the hospital records;
3.2. compare the patient's name with the name written on the immuno-haematologic test form (Annex No. 15 to Regulation No. 29 of 2004) and the hospital records;
3.3. compare the patient’s blood type to the blood type in each unit;
3.4. check the expiry date of each unit of blood and blood components;
3.5. make a visual inspection of all blood units and/or packed red blood cells and verify there are no coagula, haemolysis, abnormal colour (a sign of bacterial contamination);
3.6. make a visual inspection of the units of platelet concentrate to verify there are no aggregates or the so-called *swirling* phenomenon;
3.7. make a visual inspection of the thawed fresh frozen plasma units at 37°C to verify that there is no change in colour or presence of coagula;
3.8. return the blood product to the transfusion unit which sent it, in case of any discrepancies in the data,
3.9. determine the patient’s blood type and the type of the blood (erythrocyte concentrate) for transfusion, using test reagents anti-A, anti-B, anti-A, B;
3.10. (Amended SG Issue 37 of 2007) to carry out a compatibility test and record it in the hospital documentation:
3.10.1. in transfusion of whole blood or packed red blood cells, the compatibility test should be performed with serum (plasma) from the patient and blood from the bag;
3.10.2. in transfusion of fresh frozen plasma or platelet concentrate, the compatibility test should be performed with erythrocytes (blood) from the patient and plasma from the bag.
3.11. to control the warming process of blood units and/or packed red blood cells up to 37°C, in a thermostat or adjustable water bath.

4. Duties of the healthcare professional during blood transfusion:

4.1. blood and blood components should be transfused by intravenous transfusion using a standard transfusion system (filter pore size 170-200 μm);

4.2. at the beginning of the transfusion, a biological compatibility test should be conducted using bolus infusion of 40 ml of the blood product (from 2 to 10 ml in children), whereupon the rate of transfusion should be adjusted to 10-15 drops of blood product per minute for 5-10 minutes; if there are no objective or subjective manifestations of adverse transfusion reactions, the transfusion should continue at a rate of about 4 ml/min (if there are no restrictions for the cardiovascular system), and the blood unit or erythrocyte concentrate should get transfused for about 1-2 h;

4.3. where more than one blood unit (packed red blood cells unit) should be transfused, a biological test should be performed for each unit of the blood product.

5. Upon completion of the transfusion of blood and/or blood components, the healthcare professional should:

5.1. verify whether there have been changes in the general condition of the patient, such as blood pressure, pulse, body temperature, urine colour; if there is a change in urine colour, the healthcare professional should send a sample of it to the laboratory to test it for free haemoglobin;

5.2. fill in a transfusion form for the transfusion of blood and blood components (Annex No. 16 to Regulation No 29 of 2004);

5.3. ensure that the serum collected before the transfusion and the bag containing the rest of the blood product is stored at 4-8°C for 24 h for tests related to reactions following transfusion;

6. In case of adverse reactions and complications during blood transfusion, the healthcare professional should:

6.1. immediately terminate the transfusion of blood products;

6.2. take specific measures to control the reaction or complication depending on its type;

6.3. send the bag of blood products for microbiological testing;

6.4. send the blood samples collected from the recipient before and after transfusion of the blood product, as well as a blood sample from the bag for immuno-haematologic testing;

6.5. when samples can not be sent immediately for testing, they can be stored for up to 72h at temperatures between 4-8°C;

6.6. record any effects and complications in the form for transfusion of blood and blood components (Annex No. 16 to Regulation No. 29 of 2004);

6.7. send an immediate report by completing Annex No. 18 to Regulation No. 29 of 2004 to:

6.7.1. the hospital which sent the blood and/or blood component;

6.7.2. the committees for control of quality, safety and rational use of blood and blood components.

7. Indications for clinical use of blood and blood components

Transfusion therapy involves the administration of blood and blood components according to the nature of the disease to be treated, and on rare occasions, of whole blood.

7.1. Clinical use of whole blood

7.1.1. Indications

7.1.1.1. massive external haemorrhage with hypovolemia resulting from severe trauma or surgery;

7.1.1.2. exchange transfusion (exsanguinotransfusion).

7.1.2. Contraindications

7.1.2.1. all diseases which can be treated with blood components;

7.1.2.2. normal volemic anaemic conditions;

7.1.2.3. alloimmunization to leukocyte or platelet antigens;

7.1.2.4. alloimmunization to certain plasma proteins.

7.2. Clinical use of packed red blood cells

Packed red blood cells are used to improve the transport of oxygen from the lungs to the tissues and of carbon dioxide from the tissues to the lungs.

7.2.1. Standard packed red blood cells

7.2.1.1. Indications

7.2.1.1.1. acute bleeding in patients with normal blood values;

7.2.1.1.2. chronic anaemic conditions;

7.2.1.1.3. surgery in patients with a chronic anaemic condition.

7.2.1.2. Contraindications

7.2.1.2.1. chronic anaemic condition subject to drug therapy (iron preparations, vitamin B12, folic acid, erythropoietin);

7.2.1.2.2. alloimunization to leukocyte or platelet antigens and febrile non-haemolytic reactions;

7.2.1.2.3. immunization to plasma proteins and evidence of severe allergic reactions;

7.2.1.2.4. immunocompromised patients and patients awaiting organ, tissue or cell transplantation;

7.2.1.2.5. paroxysmal nocturnal hemoglobinuria.

7.2.2. Packed red blood cells with removed buffy-coat. This procedure is used to remove the majority of the leukocytes and platelets from the packed red blood cells.

7.2.2.1. Indications

7.2.2.1.1. the same as with the standard packed red blood cells

7.2.2.1.2. patients with febrile non-haemolytic reactions

7.2.2.2. Contraindications: the same as with the standard red cell concentrates

7.2.3. Leukocyte-depleted packed red blood cells. The use of leukocyte inactivating filters removes virtually all leukocytes from the packed red blood cells.

7.2.3.1. Indications

7.2.3.1.1. the same as with the standard packed red blood cells

7.2.3.1.2. when patients should avoid alloimmunization to HLA-antigens (e.g. chronic recipients of packed red blood cells, such as patients with thalassemia, aplastic anaemia, leukaemia, immunocompromised patients and patients subject to transplantation of haematopoietic stem cells)

7.2. 3.1.3. in patients with known alloimmunization to HLA-antigens and non-haemolytic febrile reactions;

7.2.3.1.4. in patients who need to be administered packed red blood cells negative for cytomegalovirus.

7.2.3.2. Contraindications: the same as with the standard packed red blood cells.

7.2.4. Packed red blood cells with additive (optional) solutions. The addition of a blood conserving solution reduces the content of the plasma in the packed red blood cells.

7.2.4.1. Indications: the same as with the standard packed red blood cells.

7.2.4.2. Contraindications: the same as with the standard packed red blood cells.

7.2.5. Washed packed red blood cells. The washing procedures remove plasma proteins and most of the leukocytes.

7.2.5.1. Indications

7.2.5.1.1. in patients with known antibodies to plasma proteins, mainly against immunoglobulin class A (IgA) and severe allergic reactions;

7.2.5.1.2. paroxysmal nocturnal hemoglobinuria (removal of complement);

7.2.5.1.3. packed red blood cells of blood type 0 in intrauterine transfusion.

7.2.5.2. Contraindications: the same as with the standard packed red blood cells.

7.2.6. Frozen packed red blood cells.

Frozen erythrocyte concentrates can be stored for more than 10 years.

7.2.6.1. Indications: adjustment of anaemic conditions in:

7.2.6.1.1. patients with rare blood groups;

7.2.6.1.2. patients with alloimunization to multiple red cell antigens;

7.2.6.1.3. in the absence of CMV-negative packed red blood cells or compatible leukocyte-depleted packed red blood cells. Frozen packed red blood cells stored for at least 6 months can be used for immunization against human erythrocyte antigens after retesting the donor for transmissible infection and known negative results.

7.2.6.2. Contraindications: the same as with the standard packed red blood cells

7.2.7. Irradiated packed red blood cells.

Irradiation of packed red blood cells eliminates the possibility of engraftment of T-lymphocytes in immunocompromised patients.

7.2.7.1. Indications

7.2.7.1.1. Transplantation of haematopoietic stem cells;

7.2.7.1.2. severe immune deficiency syndrome;

7.2.7.1.3. patients with immunosuppressive therapy (leukaemia, lymphomas, carcinomas);

7.2.7.1.4. intrauterine transfusions;

7.2.7.1.5. premature babies;

7.2.7.1.6. transfusions from close relatives.

7.2.7.2. Contraindications: the same as with the standard packed red blood cells.

7.3. Criteria for administration and dosage of packed red blood cells;

7.3.1. The threshold haemoglobin concentrations, requiring transfusion of packed red blood cells are:

7.3.1.1. in young healthy people: 60 to 70 g/l;

7.3.1.2. in young patients with other uncomplicated diseases (e.g. diabetes): 70-80 g/l;

7.3.1.3. in healthy adult patients (over 65 years): 90 g/l;

7.3.1.4. in patients with heart diseases, increased oxygen consumption (e.g., septicaemia): 100 g/l;

7.3.2. Dosage

7.3.2.1. acute bleeding: according to the degree of bleeding;

7.3.2.2. chronic anaemic condition: according to the degree of anaemia and clinical manifestations, most often 1E packed red blood cells a day.

7.3.3. Selection of packed red blood cells;

7.3.3.1. packed red blood cells are selected according to the recipient's blood type and the ABO and Rh-antigenic systems;

7.3.3.2. in special cases (thalassemia, chronic recipients subject to haematopoietic stem cell transplantation), packed red blood cells can be selected by phenotype and other red cell antigen systems.

7.4. Evaluation of the results from the use of packed red blood cells

7.4.1. improvement of the anaemic syndrome features;

7.4.2. increase of haemoglobin concentrations.

8. Clinical use of platelet concentrates.

Platelet concentrates are used in bleeding disorders due to reduced platelet count or impaired platelet function. They are used in the treatment and prevention of bleeding disorders.

Platelet concentrates are used to treat bleeding episodes in patients with severe thrombocytopenia (less than 10-20 x 10^9/l) or impaired platelet function and normal platelet counts.

Platelet concentrates are used for prevention of bleeding in patients with severe thrombocytopenia or impaired platelet function, and surgical interventions or invasive procedures, or short-term severe hypoproductive thrombocytopenia (less than 5-10 x 10^9/l) (leukaemia; cell, tissue or organ transplantation).

8.1. Standard platelet concentrates

8.1.1. Indications

8.1.1.1. thrombocytopenia due to impaired platelets production;

8.1.1.2. hypersplenic thrombocytopenia;

8.1.1.3. thrombocytopenia with disseminated intravascular coagulation syndrome;

8.1.1.4. thrombocytopenia with massive transfusions and cardiopulmonary bypass;

8.1.1.5. alloimmune neonatal purpura (from a compatible donor or mother);

8.1.1.6. autoimmune thrombocytopenic purpura (in life-threatening bleeding);

8.1.1.7. diseases with impaired platelet functions.

8.1.2. Contraindications

8.1.2.1. thrombotic thrombocytopenic purpura;

8.1.2.2. post-transfusion purpura;

8.1.2.3. heparin-induced thrombocytopenia.

8.2. Platelet concentrates obtained by aphaeresis (from a single donor);

8.2.1. Indications

8.2.1.1. thrombocytopenic conditions in alloimmunized patients;

8.2.1.2. thrombocytopenia in patients with immunodeficiency.

8.3. Irradiated platelet concentrates

8.3.1. Indications

8.3.1.1. thrombocytopenia in patients with compromised immunity;

8.3.1.2. transplantation of haematopoietic stem cells;

8.3.1.3. patients undergoing myeloablative therapy;

8.3.1.4. infants with massive transfusions;

8.3.1.5. premature babies;

8.3.1.6. kinship with donors.

8.4. Washed platelet concentrates

8.4.1. Indications: patients with known antibodies to plasma proteins (anti IgA-antibodies in patients with IgA-immunoglobulin deficiency).

8.5. Leukocyte-depleted platelet concentrates

8.5.1. Indications

8.5.1.1. patients with febrile non-haemolytic reactions;

8.5.1.2. prevention of alloimmunization in patients undergoing organ or cell transplantation, or chronic recipients of blood products.

8.6. Frozen platelet concentrates

8.6.1. Indications

8.6.1.1. use of a HLA and HPA compatible platelet concentrates where there is no compatible donor to obtain fresh platelet concentrates;

8.6.1.2. autologous platelet concentrates.

8.7. Platelet concentrates dosage

8.7.1. Bleeding episodes treatment: 1 platelet concentrate unit per 5-10 kg of body weight, depending on the type of thrombocytopenia and the severity of the bleeding.

8.7.2. Bleeding prevention: 1 platelet concentrate unit per 10 kg of body weight, every other day.

8.7.3. Benchmarks:

8.7.3.1. Prevention

8.7.3.1.1. threshold (*) platelet count: less than $10x10^9$/l

8.7.3.1.2. target (**) of platelet count: more than $25x10^9$/l

8.7.3.1.3. target platelet count in surgeries: more than 50-80x10/l

8.7.3.1.4. quantity of transfused platelets: more than $4x10^{11}$

8.7.3.2. Therapy

8.7.3.2.1. threshold platelet count: individual

8.7.3.2.2. target platelet count: more than $40x10^9$/l;

8.7.3.2.3. quantity of transfused platelets: more than $6x10^{11}$

Note

(*) Threshold count: recipient's platelet count which requires administration of platelet concentrates.

(**) Target count: platelet count to be achieved in the circulation system of the recipient after the administration of platelet concentrates.

8.8. Selection of platelet concentrates

8.8.1. In patients without alloimmunization to HLA or HPA-antigens:

8.8.1.1. compatible ABO-antigen system platelet concentrates are selected;

8.8.1.2. the use of platelet concentrates obtained from Rh-positive donors of Rh-negative recipients should be avoided, especially in children and women of child-bearing age

8.8.2. In patients with alloimmunization to HLA-antigens:

8.8.2.1. the most compatible HLA and ABO platelet concentrates are selected, obtained preferably from one donor, by aphaeresis;

8.8.2.2. in the absence of compatible HLA and ABO platelet concentrates, others may be administered that are not ABO compatible;

8.8.2.3. if there is a known specificity of the antibodies in HLA or HPA antigen systems, platelet concentrates should be selected according to their compatibility with the specific antigens.

8.8.3. In neonatal alloimmune purpura, platelet concentrates obtained from maternal plasma should be used, after the plasma is removed and AB blood type plasma or suitable electrolyte solution is added;

8.9. Evaluation of the results of the use of platelet concentrates

8.9.1. in thrombocytopenia

8.9.1.1. according to clinical features;

8.9.1.2. according to the adjusted increase in the platelet count

$$\text{Adjusted increase of platelets} = \frac{\text{Post-transfusion count} - \text{Pre-transfusion count}}{\text{Transfused platelet count (10(11))}} \times \text{BSA (sq.m.)}$$

BSA – Body surface area

Minimum desirable values of the adjusted increase in platelets

- 1 h after transfusion of platelet concentrates: over 5-7.5x10^9/l;
- 24 h after transfusion of platelet concentrates: over 5x10^9/l;

8.9.2. in impaired platelet function:

- according to clinical features
- according to adjustment of prolonged bleeding time.

9. Clinical use of granulocyte concentrates

Granulocyte concentrates are suspension concentrates of granulocytes in the plasma obtained by aphaeresis. Phagocytosis of microorganisms and fungi from granulocytes is used.

9.1. Indications: limited

9.1.1. Patients with severe neutropenia (less than 0.5 x 10^9/l) with known sepsis, unresponsive to adequate antibiotic therapy or granulocyte colony-stimulating factor;

9.1.2. neonatal sepsis with relative neutropenia (less than 3 x 10^9/l).

9.2. Contraindications: short=term neutropenic conditions with or without an infection susceptible to antibiotic therapy

9.3. Selection of donors of granulocyte concentrates

9.3.1. compatibility with recipient according to the ABO and Rh antigenic systems (due to erythrocyte impurities)

9.3.2. in alloimmunized recipients, HLA-antigen compatibility;

9.3.3. irradiated granulocyte concentrates are used for recipients with compromised immunity

9.3.4. in CMV-negative recipients and in newborns it is advisable that the granulocyte concentrates should be from a CMV-negative donor.

9.4. Granulocyte concentrate dosage

9.4.1. in adult patients: more than 2x10^{10} granulocytes per day;

9.4.2. in newborns: 0.1 x 10^{10}/kg bodyweight per day.

9.5. Evaluation of the use of granulocyte concentrates: level of increase of granulocyte counts in the blood of the recipient.

10. Clinical use of plasma

The most commonly used type of plasma for clinical purposes is fresh frozen plasma.

10.1. Indications

10.1.1. coagulopathies for which there are no plasma preparations (deficiency of coagulation factors II, XI, XIII);

10.1.2. thrombotic thrombocytopenic purpura;

10.1.3. syndrome of disseminated intravascular coagulation;

10.1.4. massive transfusion and dilutional coagulopathy;

10.1.5. severe liver disease with impaired protein-synthesising functions;

10.1.6. antivitamin K-anticoagulant overdose;

10.1.7. antithrombin III or plasminogen deficiency;

10.1.8. C1 inhibitor deficiency;

10.1.9. exchange transfusion (exsanguinotransfusion)

10.2. Contraindications

10.2.1. coagulopathies for which there are plasma preparations;

10.2.2. volume replacement;

10.2.3. parenteral nutrition;

10.2.4. immunoglobulin substitution;

10.2.5. alloimmunization to plasma proteins.

10.3. Selection of fresh frozen plasma

10.3.1. as plasma contains natural blood type antibodies, it is selected according to the recipient's blood type;

10.3.2. in case of lack of isotype plasma, the use of plasma from other blood types is acceptable, as shown in Table 1.

Table 1:

Use of fresh frozen plasma	
Recipient's blood type	Plasma blood type
A	A, AB
B	B, AB
0	0, A, B, AB
AB	AB

10.4. Dosage

10.4.1. standard dose: 5-10 ml/kg body weight;

10.4.2. in thrombotic thrombocytopenic purpura: 30 ml/kg body weight (risk of circulatory overload!).

10.5. Evaluation of the clinical use of fresh frozen plasma

10.5.1. in coagulation disorders: clinical features (bleeding control) and determining the concentration of the coagulation factors in the plasma of the recipient;

10.5.2. in thrombotic thrombocytopenic purpura: increased platelet count; reduced lactate dehydrogenase concentration.

11. Side effects and complications from the use of blood products

11.1. post blood transfusion haemolytic reactions

11.1.1. early post blood transfusion haemolytic reactions

These are caused by intravascular or, less often, extravascular red cell destruction in case of incompatible transfusion, mostly under the ABO-antigen system.

11.1.1.1. Clinical manifestations:

11.1.1.1.1. temperature rise, with or without chills;

11.1.1.1.2. low back pain and pain at the blood transfusion site;

11.1.1.1.3. chest tightness;

11.1.1.1.4. headache, nausea, vomiting, diarrhea;

11.1.1.1.5. shock with hypotension;

11.1.1.1.6. acute renal failure;

11.1.1.1.7. DIC syndrome;

11.1.1.1.8. hemoglobinemia, hemoglobinuria.

11.1.1.2. Therapy:

11.1.1.2.1. suspension of blood transfusion;

11.1.1.2.2. blood sampling from the recipient to demonstrate haemolysis and for immuno-haematologic testing;

11.1.1.2.3. inclusion of saline infusions;

11.1.1.2.4. anti-shock therapy;

11.1.1.2.5. haemostasis adjustment;

11.1.1.2.6. exchange transfusion.

11.2. Non-haemolytic post blood transfusion effects:

11.2.1. Post blood transfusion anaphylactic reactions.

These are caused by the anti-IgA antibodies present in patients with congenital immunoglobulin class IgA.

11.2.1.1. Clinical manifestations: nausea, vomiting, abdominal cramps, diarrhoea, transient hypertension followed by hypotension, chills without fever, skin redness, shock.

11.2.1.2. Diagnosis: demonstration of IgA deficiency, and presence of specific anti-IgA antibodies.

11.2.1.3. Therapy:

11.2.1.3.1. suspension of transfusion of blood product;

11.2.1.3.2. administration of epinephrine;

11.2.1.3.3. anti-shock measures.

11.2.2. Post transfusion allergic reactions.

These are caused by the presence of antibodies to the transfusion of any allergen.

11.2.2.1. Clinical manifestations: hives, itching, restlessness, nausea, dyspnoea, hypotension, oedema of the glottis.

11.2.2.2. Therapy:

11.2.2.2.1. in mild cases, use of antihistamine preparations;

11.2.2.2.2. in severe cases, implementation of measures such as those for anaphylactic reactions: epinephrine, anti-shock measures.

11.2.3. Non-haemolytic febrile reactions

These are caused by the presence of anti-leukocyte antibodies in the recipient and presence of the respective antigens in blood product transfusions.

11.2.3.1. Clinical manifestations: fever with or without chills and no evidence of haemolysis; in severe cases: headache, nausea, vomiting, tachycardia.

11.2.3.2. Therapy:

11.2.3.2.1. suspension of blood transfusion;

11.2.3.2.2. antipyretics.

11.3. Circulatory overload

This is caused by transfusion of large volumes of blood products at great speed.

11.3.1. Clinical manifestation: manifestations of congestive heart failure.

11.3.2. Therapy:

11.3.3. suspension of the use of blood products;

11.3.4. cardiac insufficiency treatment.

11.4. Citrate intoxication and electrolyte imbalance.

These are caused by transfusion of large volumes of blood products.

11.4.1. Clinical manifestations: hypocalcaemia, hyperkalemia, metabolic acidosis.

11.4.2. Therapeutic approach: calcium chloride, hyperkalemia adjustment and acidosis adjustment.

11.5. Transfusion of bacterially contaminated blood products

Small amounts of bacteria in blood products can develop and proliferate.

11.5.1. Clinical manifestations: fever, chills, nausea and vomiting, dyspnoea, hypotension to shock, DIC syndrome, acute renal failure.

11.5.2. Therapy:

11.5.2.1. suspension of the administration of the blood product;

11.5.2.2. anti-shock therapy;

11.5.2.3. intravenous administration of broad-spectrum antibiotics;

11.5.2.4. DIC syndrome treatment.

12. Alternatives to transfusion therapy with blood components

12.1. Autologous blood transfusions.

12.2. Medicinal treatment: when there is a possibility of influencing the disease by the use of medication, it is preferable to transfusion therapy with blood or blood components.

12.2.1. Alternatives to therapy with packed red blood cells:

12.2.1.1. pharmacological effects on anaemia: medicines containing iron, B_{12}, folic acid or erythropoietin;

12.2.1.2. bleeding control: surgical methods or haemostatic medication.

12.2.2. Alternatives to therapy with platelet concentrates: medication influencing haemostasis.

12.2.3. Alternatives to therapy with granulocyte concentrates:

12.2.3.1. growth factors;

12.2.3.2. antibiotics.

12.2.4. Alternatives to therapy with plasma:

12.2.4.1. plasma products;

12.2.4.2. haemostatic medication.

13. Therapeutic haemapheresis

Therapeutic haemapheresis is a method by which a certain blood component (plasma or cell) causing a specific disorder, is removed from the circulatory system. The removal of cells is referred to as cytapheresis and the removal of plasma – as plasmapheresis.

13.1. Therapeutic cytapheresis:

13.1.1. therapeutic leukocytapheresis (leukapheresis)

Indications:

13.1.1.1. leukaemia with hyperleukocyte syndrome;

13.1.1.2. rheumatoid arthritis.

13.1.2. Therapeutic thrombocytopheresis

13.1.2.1. Thrombocythemia with distinct clinical symptoms.

13.1.3. Therapeutic erythrocytapheresis:

13.1.3.1. sickle-cell anaemia with clinical symptoms;

13.1.3.2. malaria with hyperparasitemia.

13.2. Therapeutic plasmapheresis:

13.2.1. autoimmune diseases - removal of autologous antibodies;

13.2.2. hematologic diseases;

13.2.3. metabolic diseases;

13.2.4. neurological diseases;

13.2.5. renal diseases.

Therapeutic haemapheresis is performed with the aid of cell separators and the procedure varies according to the type of equipment and the blood component that has to be separated.

Section V

Haemovigilance

1. Definition

Haemovigilance is a monitoring system based on:

1.1. continuous and standardised data collection and analysis of information;

1.2. monitoring of adverse reactions and events associated with each step of the entire process, from blood collection to blood transfusion, including blood component transfusion errors;

blood components;

1.3. collection of information on the incidence and distribution of infectious diseases markers among blood donors;

1.4. information about the total number of recipients and transfused blood components;

1.5. control measures ensuring the quality and safety of the blood and blood components.

2. Haemovigilance goals

The ultimate goal of haemovigilance is to ensure the safety of blood and blood components and to prevent recurrence of adverse reactions and events during the transfusion process.

3. Haemovigilance includes:

3.1. maintaining registers under Art. 36 of BBDBTA in accordance with Regulation No. 29 of 2004);

3.2. establishment and reporting of adverse reactions and incidents during collection, testing, processing, storage and issuing of blood and blood components;

3.3. establishment and reporting of adverse reactions and events in blood transfusion;

3.4. all measures related to the control of quality at all levels of the blood transfusion process;

3.5. preventive measures, such as continuous collection and analysis of data from all units of the transfusion chain;

3.6. collection of data relating to the selection of donors, such as frequency and reasons for deferral of donors;

3.7. collection of epidemiological data on donors with confirmed positive results from infectious markers screening;

3.8. haemovigilance system for fast and safe delivery of accurate and correct data to the competent national authority in cases of proven or suspected problems;

3.9. corrective measures relating to quarantine or return of faulty materials or products, procedures for traceability of the processes (look-back procedures);

3.10. training of staff from all departments of the transfusion chain and exchange of information.

4. Traceability of blood components

4.1. Traceability of blood components is made possible by the possibility to trace each unit of blood or blood component from the donor to its final destination, be it a recipient, a manufacturer of medicinal products from plasma, or a disposal site, and from its final destination to the donor.

4.2. Healthcare facilities providing services under BBDBTA ensure the traceability of blood and blood components through accurate identification procedures, record keeping and appropriate procedures for labelling and reporting of any serious adverse reactions and/or serious events to the competent authority.

4.3. (Amended SG, Issue 37 of 2007) BTEs and BTWs at regional hospitals should implement measures that allow traceability of blood components to their destination and processing stage.

4.4. BTEs and BTWs at regional hospitals should maintain a system for unique identification of each donor, each donated blood unit and each prepared blood component regardless of their designation, as well as of all sites to which blood components are delivered.

4.5. Healthcare facilities providing services under BBDBTA should have a system for registration of all derived units of blood and blood components, irrespective of whether they were processed at this facility or not, and for registration of the destination of the resulting blood unit, irrespective of whether it was transfused, destroyed or returned to the BTEs or BTWs that supplied it.

4.6. BTEs and BTWs at regional hospitals should have a unique identification system that allows traceability between these blood establishments and each blood units supplied by them, as well as each blood component prepared by a specific BTE.

4.7. BTEs and BTWs at regional hospitals should have a verification procedure in place for all cases in which they provide units of blood and blood components for transfusion, which procedure should certify whether a unit has been transfused to the recipient for whom it was intended, and in case it has not, to check its status.

4.8. Traceability should give information about the total number of:

4.8.1. patients who received blood or blood components;

4.8.2. units of blood or blood components that have been used;

4.8.3. donors from whom the transfused blood or blood components were obtained;

5. Types of adverse reactions in patients:

5.1. immediate reactions occurring during or immediately after transfusion, such as haemolysis, non-haemolytic febrile transfusion reactions, rash, erythema, hives, anaphylactic shock, bacterial contamination, acute lung injury associated with transfusion, etc.;

5.2. delayed side effects after blood transfusion, such as haemolysis, acute GvHD, post-transfusion purpura, increased ALT, hemochromatosis, etc.;

5.3. alloimmunisation to erythrocyte, HLA or platelet antigens;

5.4. all previously unknown side effects and events associated with the transfusion of blood components;

5.5. types of serious adverse reactions:

5.5.1. immunological haemolysis due to ABO incompatibility;

5.5.2. immunological haemolysis due to other allo-antibodies;

5.5.3. non-immunological haemolysis;

5.5.4. transfusion-transmitted bacterial infection;

5.5.5. anaphylaxis / hypersensitivity;

5.5.6. transfusion-related acute lung injury;

5.5.7. transfusion-transmitted viral infection (HBV);

5.5.8. transfusion-transmitted viral infection (HCV);

5.5.9. transfusion-transmitted viral infection (HIV-1/2);

5.5.10. transfusion-transmitted viral infection, other;

5.5.11. transfusion-transmitted parasitic infection (Malaria);

5.5.12. other parasitic infections transmitted by blood transfusion (specify);

5.5.13. post-transfusion purpura;

5.5.14. GvHD.

6. Serious adverse reactions – imputability levels

Imputability level		Explanation
NA	Not assessable	When there is insufficient data for imputability assessment
0	Excluded	When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to alternative causes
	Unlikely	When the evidence is clearly in favour of attributing the adverse reaction to causes other that the blood and blood components.
1	Possible	When the evidence is indeterminate for attributing adverse reaction either to the blood or

		blood component or to alternative causes.
2	Likely, Probable	When the evidence is clearly in favour of attributing the adverse reaction to the blood or blood component
3	Certain	When there is conclusive evidence beyond reasonable doubt for attributing the adverse reaction to the blood or blood component

7. Reporting of adverse reactions in patients:

7.1. Healthcare professionals performing transfusion and observing adverse reactions in patients with imputability level 1, 2 and 3 should immediately report such events by filling in the form contained in Annex No. 18 of Regulation 29 of 2004 to:

7.1.1. the healthcare facility which supplied the blood and/or blood component;

7.1.2. the committees for quality control, safety and rational use of blood and blood components at the healthcare facility.

7.2. (Amended SG, Issue 37 of 2007) The BTEs or BTWs at the regional hospitals which issued the blood and blood components should immediately send to the Bulgarian Executive Agency (BDA) the filled in form contained in Annex No. 18 of Regulation No. 29 of 2004 to notify it of any serious adverse reactions in patients with imputability level 2 or 3.

7.3. The committee for quality control, safety and rational use of blood and blood components at the healthcare facility should:

7.3.1. periodically (every 3 months) analyse all serious adverse reactions in patients and make an analysis of suspected serious adverse reactions according to their imputability levels;

7.3.2. confirm or reject serious adverse reactions;

7.3.3. implement prevention measures;

7.3.4. (Amended SG, Issues 37 of 2007) prepare a report containing information from the analysis and the implemented corrective and preventive measures, and send it to the healthcare facility which supplied the blood and/or blood component, and to BDA;

7.4. Based on the communications received in the form contained in Annex No. 18 from the inpatient healthcare facilities and dispensaries, BTWs at regional hospitals and BTEs must complete Section IV of Annex No. 3 of Regulation No. 29 of 2004.

8. Types of adverse reactions in donors:

8.1. adverse reactions observed during blood collection:

8.1.1. local reactions: venipuncture failure, hematoma, localized subcutaneous infections, local allergic skin reactions, accidental arterial puncture;

8.1.2. systemic reactions: light: without loss of consciousness, moderate: syncopal, heavy: convulsive.

9. Registration and reporting of adverse reactions in donors:

9.1. For each adverse reaction a form should be completed as the one in Annex No. 19 of Regulation No. 29 of 2004.

9.2. (Amended SG, Issue 37 of 2007) Serious adverse reactions in donors should be reported by completing a form as specified in 9.1 and sending it to BDA;

9.3. The summarised data associated with adverse reactions during and after blood collection should be filled in Section V of Annex No. 3 of Regulation No. 29 of 2004.

10. Serious adverse events caused during collection, testing, processing, storage and issuing of blood and blood components, which can lead to adverse reactions in recipients or donors, are:

10.1. incorrect labelling of blood samples;

10.2. inadequate testing of infectious agents;

10.3. errors in the determination of ABO blood type;

10.4. deficiencies related to the processing and storage of blood;

10.5. deficiencies related to the storage of blood components;

10.6. incorrect labelling of blood components.

11. BTWs at regional hospitals and BTEs should:

11.1. implement measures for keeping records of all serious adverse events that could affect the quality or safety of the blood and blood components;

11.2. analyse serious adverse events in order to identify preventable causes within the process and take preventive measures to avoid serious incidents;

11.3. (Amended, SG Issue 37 of 2007) send a rapid notification to BDA in the format presented below containing data about the reporting establishment, the date on which the serious adverse event occurred and the reasons that caused the accident:

	Specifications			
Serious adverse event affecting the quality and safety of the blood component due to a deviation in:	Product defect	Equipment failure	Human error	Other (specify)
Blood collection				
Aphaeresis collection				
Testing of donations				
Processing				
Storage				
Distribution				
Materials				
Others (specify)				

11.4 (Amended SG, Issue 37 of 2007) submit to BDA on an annual basis a complete report on all serious adverse events by using the form presented below:

Annual serious adverse events report form

Reporting establishment					
Reporting period		1 January – 31 December (year)			
Total quantity of processed blood and blood components					
Serious adverse event affecting the quality and safety of the blood component due to a	Total number / quantity	Specification			
		Product defect	Equipment failure	Human error	Other (specify)

deviation in:					
Aphaeresis collection					
Testing of donations					
Processing					
Storage					
Distribution					
Other (specify)					

11.5. (Amended SG, Issue 37 of 2007) if necessary, BDA should exchange information on any serious adverse reactions and serious events with the competent authorities of other countries.

11.6. (New SG, Issue 37 of 2007) not later than June 30 of the respective year, the Executive Director of BDA should submit to the European Commission an annual report on all communications of serious adverse reactions and events received over the previous year.

12. Traceability and recall of potentially infectious agents (HIV, HCV or HBV)

12.1. Post blood transfusion infections reported to BTEs and BTWs:

12.1.1. healthcare facilities should inform BTEs and BTWs when a recipient of blood products has laboratory results and/or shows symptoms of a disorder suggesting that a blood component may be hepatitis (B or C) or HIV infectious.

12.1.2. BTEs and BTWs may require reasonable clinical information from the healthcare facility about the infection and progression of the condition of the recipient.

12.1.3. BTEs and BTWs should temporarily block all related donors for future instances of blood collection; temporarily block all components from related donors available at BTEs and BTWs, and withdraw all non-expired products:

12.1.4. BTEs and BTWs should establish an investigation plan, the results of which should be documented. The investigation results of the specific donors may be reanalysed, or additional/confirmatory tests may be conducted on archived samples or new samples from the donor to rule out HIV, HCV or HBV infections in donors.

12.1.5. When positive HIV, HCV or HBV infection test results come in for a suspected donor, BTEs and BTWs should choose an adequate approach to remove the donor from blood

donation and undertake a look-back procedure of potentially infectious units which have already been taken.

13. Traceability of recipients of potentially infected blood (look-back procedure)

13.1. BTEs and BTWs implement a look-back procedure for tracing the recipients of blood components of potentially infectious blood donations and for having such recipients informed by their attending physicians when these donations could have been made in a window period by a repeated donor with confirmed HIV, HBV and HCV infection. Suspicious donations include those made in a period of time equal to the maximum window period of infection for the specific test, preceding the negative result from the screening of the donor.

13.2. BTEs and BTWs should inform in writing the healthcare facility of the event and advise the facility to trace all recipients of suspicious blood components, as well as inform the healthcare professional about potentially infectious blood transfusion.

13.3. It is the healthcare professional's responsibility to inform the recipient of the potential risk of infectious blood transfusion, unless there are medical reasons not to do so. If the recipient has been tested to establish or rule out an infection, BTEs and BTWS should be informed of the test results. If the recipient has not been tested, BTEs and BTWs should also be informed by the healthcare facility.

Section VI

Quality System

1. BTEs and BTWs should establish a quality system. It should contain descriptions of at least the following processes:

1.1. quality management, quality assurance, continuous quality improvement, change control and validation processes;

1.2. personnel and organization;

1.3. premises and equipment;

1.4. documentation;

1.5. blood and blood components;

1.6. testing and processing of blood and blood components;

1.7. storage, issuing and distribution of blood and blood components;

1.8. quality monitoring;

1.9. quality control;

1.10. deviations, complaints, adverse events or reactions, withdrawal of blood, corrective and preventive measures;

1.11. self-inspections, audits and quality improvement;

1.12. contract management.

2. Quality management, change control and validation processes

2.1. Management's responsibilities - management bodies at BTEs and BTWs should establish a policy for achieving and maintaining quality.

2.2. Organization - BTEs and BTWs should have an organizational structure that works for the achievement of the goals of the quality policy.

2.3. Methods of achieving quality: BTEs should have all required means to produce blood components consistent with the predefined quality objectives.

2.4. Person responsible for quality:

2.4.1. All BTEs should have a quality assurance (QA) unit managed by a responsible person subordinated directly to the Director. The unit should be formed as a separate structure in the structure of BTEs or as a working group of experts belonging to different departments.

2.4.2. The functions of the QA unit include the following:

2.4.2.1. review and approval of standard operating protocols, training plans, development of new processes;

2.4.2.2. review and approval of process validation, validation plans and validation results;

2.4.2.3. review and approval of document control;

2.4.2.4. batch release approval;

2.4.2.5. system checks;

2.4.2.6. review and approval of corrective measure plans;

2.4.2.7. development of criteria for assessment of systems and trends;

2.4.2.8. monitoring problems such as error and incident reports, annual reports, corrective and preventive measures.

2.5. In all BTWs, the QA unit should be formed on a functional basis, and the tasks of each employee should be defined by the Head of the Department in accordance with paragraph 2.4.2.

2.6. Process validation: all BTEs and BTWS should develop rules for the validation of equipment, facilities, processes, automated systems and laboratory tests, periodically, at regular intervals defined as a result of these activities.

3. Personnel and organization

3.1. All BTEs and BTWs should establish a procedure for selection of well-qualified personnel with appropriate education, training and experience.

3.2. Job descriptions should be compiled for each job position, reflecting the tasks, responsibilities and skills, as well as the training, knowledge and experience required for the specific position.

3.3. All BTEs and BTWs should create a training program to verify the competence of their staff. Training and inspections should be planned and documented.

3.4. Training programs should be reviewed and updated periodically.

3.5. Personnel competence should be checked regularly.

3.6. Instructions suitable for the specific operations should be developed to ensure safe work and hygiene.

4. Premises and equipment

4.1. Premises

4.1.1. All BTEs and BTWs should be designed, constructed and/or adapted so that the production of blood components will be secure and of high quality.

4.1.2. The layout of the premises and their furnishings should be selected so as to minimize the possibility of errors.

4.1.3. If possible, the premises should be planned in such a way that each operation can be performed in the specific order, avoiding crossing of flows.

4.1.4. (Amended SG, Issue 92 of 2010) Separate rooms are needed for donor selection, including space for confidential interviews with prospective donors, blood collection, blood processing, laboratory testing, storage of materials, reagents and blood products.

4.2. Equipment

4.2.1. Equipment should be designed, validated and maintained so as to meet its intended purpose and not be a risk to donors, blood components or the personnel.

4.2.2. A programme and a timetable for validation, calibration and preventive maintenance should be developed for all devices, equipment and instrumentation.

4.2.3. All protocols for maintenance, repair, calibration and revalidation should be stored and periodically reviewed.

5. Documentation

5.1. BTE and BTW documentation should cover at least:

5.1.1. Quality manual.

5.1.2. Specifications of the used materials, reagents, equipment, blood components.

5.1.3. Standard operating protocols for all critical processes and procedures.

5.1.4. Work instructions.

5.1.5. Procedure documenting logbooks.

5.1.6. IT systems description

5.1.7. Inspection reports, claims, errors and incidents.

5.1.8. Personnel training protocols.

5.1.9. Information leaflets for products intended for end-users.

5.2. Effective control of the documentation at BTEs and BTWs is achieved through a well-defined structure capable of providing links between the implemented quality policy and the description of all processes, procedures, forms and working papers in a well-organized operating system.

5.3. Documents development

5.3.1. All BTEs and BTWs should establish procedures governing the ways in which records are prepared and maintained.

5.3.2. Before the entry of a new document, the procedures described in it should be validated.

5.3.3. Data protection rules should be observed in the preparation of documents.

5.3.4. All documents related to donor selection and to reception and quality control of blood components should be stored for not less than 30 years.

6. Collection of blood and blood components

Blood collection procedures should be monitored closely by providing:

6.1. Full identification of donors and units.

6.2. Inspection of blood collection systems for defects and impurities prior to use.

6.3. Treatment and disinfection of the injection site, blood collection, control samples collection, identification of blood units and control samples, as well as the documentation of all control parameters should be carried out according to validated standard operating protocols.

6.4. Proper storage and transportation of blood units prior to processing.

7. Receipt of blood components

7.1. BTEs should develop specifications for the materials used for blood collection and processing.

7.2. BTEs should define the quality parameters for the manufactured blood components. The following parameters should be defined for each component:

7.2.1. Component definition

7.2.2. Properties: therapeutic elements, quantity, presence of other products or cells.

7.2.3. Collection method with a description of the basic technological principles.

7.2.4. Labelling.

7.2.5. User information on blood components.

7.2.6. Storage conditions and shelf life.

7.2.7. Quality assurance and inclusion of all required parameters of the individual components, frequency of quality control tests, and number of tested units.

7.2.8. Transportation of units to healthcare facilities.

7.3. BTEs should develop and observe standard operating protocols for all activities in their production chain, from receipt of donated blood units for processing until their issuing.

7.4. BTEs should develop procedures to control the introduction of changes in processes and procedures.

7.5. BTEs should validate all processes and procedures retrospectively or prospectively.

7.6. BTEs should monitor and control all manufacturing processes.

7.7. BTEs should develop quality control and monitoring plans for blood components.

7.8. BTEs should define the requirements for the suppliers of raw materials, reagents, consumables, equipment.

7.9. BTEs should develop a control system for out-of-specification products.

7.10. BTEs should implement a system for statistical control of manufacturing processes.

8. Storage and issuing of blood and blood components

8.1. Storage and issuing of blood and blood components should be performed in a way that ensures their quality throughout the storage period and prevents mix-ups.

8.2. A system should be in place for maintenance and control of the storage conditions of all units of blood and blood components throughout their shelf life, including during transportation.

8.3. The temperature levels and hygiene of the storage areas for blood and blood components should be monitored regularly.

8.4. Autologous donations of blood and blood components should be kept in clearly designated areas, separately from the homologous units.

8.5. Issuing of blood and blood components

8.5.1. Before issuing, a visual inspection of the units should be performed. Records should be kept for the units that are issued and received.

8.5.2. Issued blood components should not be accepted for re-issuing except when:

8.5.2.1. the return procedure for blood components is agreed in a contract;

8.5.2.2. there is evidence for each blood component showing that the storage conditions have been met;

8.5.2.3. there is enough material to perform a compatibility test.

8.5.3. Before re-issuing of blood components records should be kept certifying that a visual inspection of the components has been made.

9. Quality monitoring

9.1. BTEs should maintain a database to validate each step of the manufacturing processes.

9.2. BTEs should validate all critical processes.

9.3. BTEs should maintain a database for quality control.

9.4. Eligibility criteria for use of blood components should be based on their specifications.

10. Quality control

10.1. BTEs should provide sufficient qualified personnel, independent of the direct manufacturing processes, adequate facilities and equipment to carry out the required testing of materials and products.

10.2. Sampling and testing should be carried out in compliance with well-defined operating procedures.

10.3. All methods and quality control procedures should be validated.

10.4. Quality control documentation should clearly show that all required tests have been carried out and that the test results for the specific materials and products meet the established specifications.

10.5. All reasons for deviation from the established requirements should be documented and investigated.

10.6. Quality control should cover all processes in the transfusion chain affecting the quality of the final products:

10.6.1. control of incoming materials;

10.6.2. control of equipment and premises;

10.6.3. control of laboratory tests;

10.6.4. control of products;

10.6.5. control of information systems;

10.6.6. document control.

11. Deviations, complaints, adverse events or reactions, withdrawal of blood and blood components, corrective and preventive measures

11.1. Healthcare facilities that collect, process, store, issue or transfuse blood components, should establish a system to document errors and incidents.

11.2. All complaints and any information suggesting that defective blood components have been issued should be carefully examined. Written procedures should be established for blocking and withdrawal of defective blood components or blood components with suspected defects.

11.3. Complaints: healthcare facilities should establish a system for investigation and analysis of all complaints from donors and recipients.

11.4. Returned blood components: BTEs and BTWs should assign responsible persons for the investigation and analysis of complaints from recipients of blood components.

11.5. Withdrawal of blood and blood components

11.5.1. BTEs and BTWs should establish a mechanism by which issued blood components or components with suspected defects can rapidly be blocked and withdrawn.

11.5.2. The decision to withdraw blood and blood components stored in BTEs should be taken by the director of the BTE on the basis of the opinion of a specially appointed committee.

11.5.3. The decision to withdraw blood and blood components stored in healthcare facilities outside BTEs should be taken by the commission under Article 41 of the BBDBTA on the advice of a doctor or nurse who found discrepancies with the blood transfusion standards.

12. Self-inspections, audits and quality improvement

12.1. BTEs and BTWs should establish a system for internal audits and self-inspections.

12.2. Self-inspections and internal audits should only be carried out by trained and competent professionals from within the organization.

12.3. Self-inspections and internal audits should be carried out according to protocols approved in advance.

12.4. All results of inspection and internal controls should be documented and reported to management of BTEs and BTWs.

12.5. The preventive and corrective measures undertaken to improve quality should be documented and their effectiveness verified.

12.6. BTEs and BTWs should establish a system for continuous quality improvement.

13. The tasks performed by external organizations should be defined explicitly in a written contract.

Section VII

Rights of donors and patients and protection of medical and non-medical professionals

1. Rights of donors

Each donor has the right to:

1.1. equality in terms of gender, social status, religion;

1.2. obtain information about the collection of blood or blood components, the physiological changes that occur in the body as a result of that, the safety precautions and potential risks, according to Section IV, paragraph I. Requirements for donor selection and blood collection;

1.3. obtain information about their health after the examination, and the results of the laboratory tests

1.4. contact the head of the blood collection team in private;

1.5. be supervised and cared for during blood donation and after that, until a satisfactory status is confirmed;

1.6. get advice on how to treat the phlebotomy site;

1.7. obtain instructions on how to proceed in the next 3 days;

1.8. eat energising foods after blood collection.

2. Any patient who meets the indications for inclusion in an individual autologous transfusion is entitled to receive information about:

2.1. the blood or blood components collection procedure, the changes that occur in the body as a result of the procedure, the safety precautions and potential risks according to Section IV, paragraph I - requirements for donor selection and blood collection;

2.2. the protocols used in autologous transfusion;

2.3. the advantages of autologous transfusion;

2.4. the results of the tests performed on the collected blood or blood components;

2.5. the clinical status which allows the patient to participate in the program for autologous transfusion;

2.6. to refuse to be included in an individual autologous transfusion programme.

3. Each recipient has the right to:

3.1. equality in terms of gender, social status, religion;

3.2. obtain information from the healthcare professional:

3.2.1. about the reasons requiring transfusion of blood and blood components;

3.2.2. about the purpose of the transfusion and the expected results;

3.2.3. about the nature of the "transfusion" procedure

3.2.4. about possible side effects and potential risks associated with the transfusion of blood and blood components;

3.2.5. about available alternatives;

3.3. refuse blood transfusion;

3.4. be supervised and cared for during blood transfusion and after that until a satisfactory status is confirmed by the healthcare professional.

4. Protection of medical and non-medical professionals

All employees working in healthcare facilities providing services under BBDBTA have the right to:

4.1. education and training, access to scientific and technical achievements;

4.2. ethical relationships;

4.3. preservation of their human dignity and professional opinion;

4.4. safe, hygienic and healthy work conditions;

4.5. a fair evaluation of their work;

4.6. participation in communication, analysis and publication of the results of the operations;

4.7. information and training in Transfusion Haematology and other specialties related to Transfusion Haematology;

4.8. a motivated refusal to carry out tests and manipulations on unsuitable or unfit biological materials.

I, the undersigned Maria Georgieva Eneva, hereby certify that this is a full, true and accurate translation from Bulgarian into English of the attached document: Regulation No. 9.
The translation consists of 79 (seventy-nine) pages.
Translator: Maria Georgieva Eneva